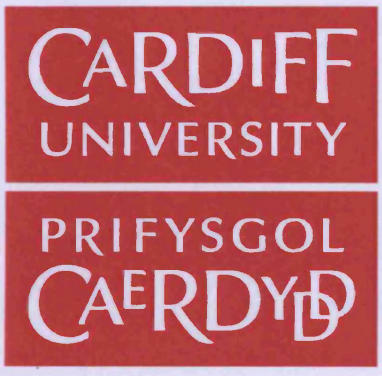
Two Approaches to New Chiral Selenenylating Reagents



A Thesis Submitted to Cardiff University

in Fulfilment of the Requirements for the Degree of

Doctor of Philosophy

by Diana Maria Freudendahl

PhD Thesis November 2010
Cardiff University

ProQuest LLC
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106-1346

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Dedicated to my Parents, my Husband
and a Little Star.

Acknowledgements

I am indebted to many people for their long-lasting support and encouragement which was invaluable for the successful completion of this research work. In the following lines some of them are gratefully acknowledged. However, I am aware of the fact that there are many more and these words cannot express the gratitude and respect I feel for all of them.

Firstly, I would like to take this opportunity to thank my supervisor Professor Thomas Wirth who gave me the opportunity to "play around" with selenium chemistry. He offered me a warm welcome in his group and always generously offered advice, especially when I, every now and then, stumbled upon odd results.

My sincere thanks go to many friends and colleagues for scientific discussion, advice and continuous support, among them Dr. Sascha Schäfer, Dr. Sohail A. Shahzad, Johan Brandt and Dr. Rob Richardson, for many valuable ideas and suggestions. I am also grateful to Danielle Browne who introduced me to the "secrets" of selenium chemistry and Zaho Liwei to whom I owe the greatest thanks for his help in the lab.

I also had the great pleasure to work with Simon Elmore, Umar Farid, Zulfiqar A. Khan, Yvonne Luk, Omar Elhady, Kevin Watts, Bukkola Ojo, Dr. Sabine Altermann, Dr. Rasheed Munawwer, Dr. Fateh V. Singh, Dr. Azhar ul Haq Ali Shah, Dr. Umar Farooq and the "Allemann-team": James Johnston, George May, Sarah Adams and Dr. Robert Mart. We had good fun!

Many thanks go to the visiting students, of whom I here can just mention a few: Julien Espace, Hobalah Bouzid, Christoph Rosorius, Guillaume Marie, Margerita Villegas, and Ahmed Hammami.

Special thanks go to my former colleagues Marcel Sickert and Anica Dose - although far away, they were always very encouraging and helpful in science and life in general.

In order to get this thesis to a readable state some people had to endure some suffering, many thanks for your endurance: Marcel, Charlotte, Kathrin, Sascha, Anica, Sabine, Manna and Johannes.

I would like to acknowledge Prof. Michio Iwaoka, Prof. Claudio Santi and Prof. Andrew French, who came to Cardiff as visiting professors or guest lecturers and were always generous with their advice.

Grateful thanks are going to Prof. G. Mugesh, who gave me the opportunity to stay for some weeks with his group at the Indian Institute of Science, Bangalore. I felt always welcomed by him and his students: Dr. Tamil Selvi, Dr. Krishna Pada Bhabak, Debasish Manna, Bhaskar Jyoti Bhuyan, Debasish Bhowmick, M. Umayal and Surendan Reddy Jakka.

Thanks to the lecturers Mike Coogan and Niek Buurma for their encouragement and suggestions during my six-monthly vivas and to Nick Tomkinson for his good advice.

My acknowledgements would remain incomplete if I did not mention the support of technical and non-technical staff at the School of Chemistry, especially, Rob Jenkins, Sham Ali and Alun Davies. I

also want to thank the EPSRC National Mass Spectrometry Service Centre (Swansea) for mass spectrometric data and the EPSRC X-Ray Crystallography Service Centre (Southampton) and Dr. B. Kariuki (Cardiff University) for the X-Ray analysis.

Finally, I am grateful to Cardiff University and the UKIERI-Scheme for the generous financial support, without which this thesis would not have been possible.

Last but by no means least, I would like to thank my family for the opportunity to start and pursue a career in science. I am particularly indebted to my parents for their never-ending encouragement and ongoing support. Very special thanks go to my beloved husband for his moral support and patience. He always brought me back when I found myself lost in the depths of chemistry, the universe and everything. Don't panic!

Diana M. Freudendahl

The most exciting phrase to hear in science, the one that heralds the most discoveries, is not "Eureka!", but "That's funny..."

~Isaac Asimov

Abstract

Selenium electrophiles are useful reagents for chemo- and stereoselective functionalisations of carbon-carbon double and triple bonds.

In this thesis, two approaches to novel selenenylating reagents are presented. In a "classical" approach several new chiral diselenides are prepared and their corresponding selenium electrophiles are used for the stereoselective functionalisations of alkenes. These new diselenides contain sulfoxide or sulfone moieties in coordinative distance to the selenium atoms. The influence of solvents, alkenes and different nucleophiles on the outcome of selenenylation reactions using the corresponding new selenium electrophiles is studied. It can be shown that diastereomeric ratios up to 92:8 can be achieved.

Besides the successful selenenylation reactions, one selenium electrophile bearing a sulfoxide moiety shows an unexpected reactivity, forming six-membered heterocyclic systems upon reaction with alkenes. A mechanism for the formation of these 2,3-dihydro-1,4-benzoselenothiine-1-oxides is proposed.

The second approach presented uses the concept of asymmetric counteranion directed catalysis (ACDC) as tool for influencing the stereoselective outcome of selenenylation reactions. Several reactions using unfunctionalised, functionalised or chiral selenium electrophiles together with different chiral organic acids are shown.

Additionally, some results are presented highlighting the use of three of the new diselenides as glutathione peroxidase mimics.

List of Abbreviations

°C	Degree Celsius
Å	Angstrøm
Ac	Acetyl
acac	Acetylacetonate
Ar	Aryl
ACDC	Asymmetric Counteranion Directed Catalysis
AgBINOL-P	1,1'-Binaphthyl-2,2'-diyl silver phosphate
atm	Atmosphere
BINOL	1,1'-Bi-2,2'-naphthol
BINOL-P	1,1'-Binaphthyl-2,2'-diyl hydrogen phosphate
BuOH	Butanol
CHP	Cumyl hydroperoxide
CPME	Cyclopentyl methyl ether
δ	Chemical shift
d.e.	Diastereomeric excess
d.r.	Diastereomeric ratio
DET	Diethyl tartrate
(+)–DIP-Cl	(+)-Diisopinocampheyl chloroborane
dl	Decilitres
DMAP	4-Dimethylaminopyridine
DMF	*N*,*N*-Dimethylformamide
dppm	1,1-Bis(diphenylphosphino)methane
e.e.	Enantiomeric excess
e.r.	Enantiomeric ratio
EI	Electron impact ionisation
ESI	Electrospray ionisation
Et	Ethyl
EtOH	Ethanol
GP	General procedure
GPx	Glutathione peroxidase
GSH	Glutathione
h	Hour/hours
HPLC	High pressure liquid chromatography
HRMS	High resolution mass spectrometry
Hz	Hertz
ID	Iodothyronine deiodinase
Im_2CO	1,1'-carbonylbiimidazole

i-Pr	*i*-Propyl
l	Litre
LDA	Lithium diisopropylamide
LiTMP	Lithium 2,2,4,4-tetramethylpiperidine
M	Molarity (mol/l)
m-CPBA	3-Chloroperoxybenzoic acid
Me	Methyl
MeLi	Methyllithium
MeOH	Methanol
Ms	Methanesulfonyl
µg	Microgram
MHz	Megahertz
min	Minute
ml	Millilitre
mmol	Millimol
m.p.	Melting point
MTBE	Methyl *t*-butyl ether
m/z	Mass over charge ratio
n-BuLi	*n*-Butyllithium
NMR	Nuclear magnetic resonance
ppm	Parts per million
Ph	Phenyl
Pr	Propyl
PrOH	Propanol
R_F	Retention factor
SPINOL	1,1'-Spirobiindande-7,7'-diol
SPINOL-P	1,1'-Spirobiindande-7,7'-diyl hydrogen phosphate
t-Bu	*t*-Butyl
t-BuLi	*t*-Butyllithium
t-BuOH	*t*-Butanol
TBHP	*t*-Butyl hydroperoxide
THF	Tetrahydrofuran
TMEDA	*N,N,N',N'*-Tetramethylethylenediamine
p-TsCl	4-Toluenesulfonyl chloride
r.t.	Room temperature
TLC	Thin layer chromatography
TRIP	3,3'-Bis(2,4,6-triisopropylphenyl)- 1,1'-binaphthyl-2,2'-diyl hydrogen phosphate
TrxR	Thioredoxin reductase

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1. Introduction

1.1 Selenium

Selenium was first identified in 1817 by the Swedish chemist Jöns Jakob Berzelius (1779-1848). Berzelius and his colleague Johan Gottlieb Gahn (1745-1818) were studying red-brown sediments in lead chambers which were used for the production of sulfuric acid in a plant at Gripsholm (Sweden). They identified a substance with a very intense scent and, at first, thought it was tellurium. However, a more careful analysis revealed a new substance, which was given the name selenium, a term that derives from the Greek word for moon – *selènè*. Berzelius thought it appropriate to name the element for the earth's satellite, since Klaproth had named the closely related element tellurium after the Latin word – *tellus* – for the earth.

Selenium's atomic number is 34 and the average mass is 78.96 atomic mass units. The main isotopes are ^{78}Se and ^{80}Se with 24% and 50% natural occurrence. Selenium is chemically closely related to sulfur and tellurium and is often found associated with sulfur. It can be found in economic quantities in sulfide ores such as pyrites where it partially replaces sulfur in the ore matrix. Elemental selenium exists in a variety of modifications: a black glass-like allotrope, a grey metallic shape, formed by long chains and showing electric conductivity, and several red non-metallic crystalline appearances, consisting of Se_8 rings or further amorphous or glassy modifications.

The electric conductivity of grey selenium is greatly affected by the amount of light shining on it. The brighter the light, the better selenium conducts electricity. This property has made selenium useful in devices that respond to the intensity of light, such as electric dyes, photo cells, light meters for cameras and copiers. Selenium can also produce electricity directly from sunlight and is therefore used in solar cells. The element is also a semiconductor and is used in some types of solid-state electronics. In addition to its use in electrical devices, selenium is also used to make a ruby-red colour in glasses and enamels, as a photographic toner and as an additive to stainless steel.

1.2 Organoselenium Chemistry

The first organoselenium compound – ethyl selenol – was already synthesised in 1847, by Wöhler and Siemens. Although the use of selenium dioxide as stoichiometric oxidant in synthetic chemistry appeared already in 1929 as a patent by the I. G. Farbenindustrie AG, it took more than 120 years from the first synthesis of an organoselenium compound until real interest in this chemistry arose. The discovery of the selenoxide elimination in 1970 marked a major breakthrough for the development of organoselenium chemistry.[1] Since that time selenium-based methods in organic chemistry have developed rapidly, and in 1988 the first chiral selenium reagent was synthesised by Tomoda.[2]

Selenium, in organoselenium reagents, prefers bivalent (selenides or diselenides) over tetravalent bonding (e.g. seleninic acids). The names of the most commonly used organoselenium species are listed in Table 1.1.

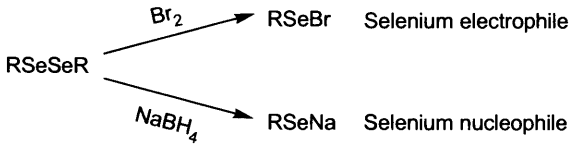
Table 1.1: *Names of functional groups of common organoselenium reagents*

Functional group	Reagent name
R-SeH	selenol
R-Se-R'	selenide
R-SeCN	selenocyanate
R-SeX	selenenyl halide
R-Se-Se-R'	diselenide
R-SeOH	selenenic acid
R-Se(O)-R'	selenoxide
R-Se(O)-OH	seleninic acid
$R\text{-}SeX_3$	selenenyl trihalide
$R\text{-}Se(O)_2\text{-}OH$	selenonic acid

The carbon-selenium bond length (C-Se bond: 198 pm) and energies (C-Se bond: 243 kJ/mol) of organoselenium compounds are typically longer and of lower energies than the corresponding carbon-sulfur bonds (C-S bond: 181 pm and 272 kJ/mol) in organosulfur compounds.[3] These attributes are responsible for a higher reactivity, compared to the organosulfur compounds and allow therefore milder reaction conditions.

Organoselenium compounds are useful reagents to achieve chemo-, regio- and stereoselective functionalisations of complex organic substrates. It is possible to introduce selenium as an electrophile, a nucleophile or as a radical. Conversion into various functional groups can be attained directly, or after further manipulation of the selenium containing molecule. The incorporated organoselenium moiety can be easily attacked by nucleophiles, or converted into radicals by homolytic

cleavage.[4] Oxidation to the selenoxide and subsequent β-elimination allows the introduction of double bonds.[5] A further characteristic of organoselenium species involves the reaction of the selenide with a suitable organolithium compound, which allows the formation of a carbanion by α-deprotonation. Important precursors for reactive organoselenium compounds like selenium electrophiles and selenium nucleophiles are diselenides. Two typical reactions are shown in Scheme 1.1.



Scheme 1.1: *Generation of selenium electrophiles and nucleophiles using diselenides*

Some important chiral diselenides which were successfully synthesised and transformed into the corresponding reactive species are shown in Figure 1.1. Most of these diselenides are C_2-symmetric and can be obtained easily from commercially available precursors.

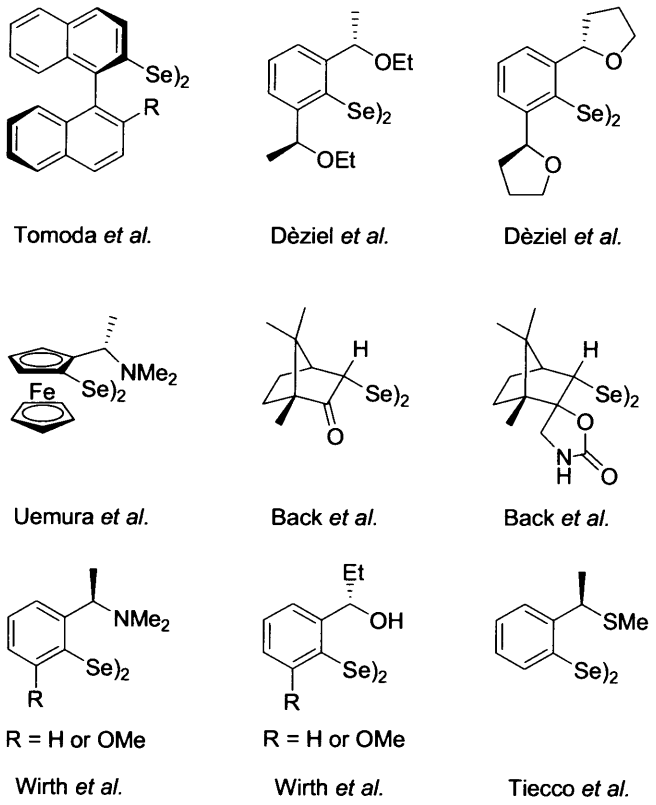


Figure 1.1: *Chiral diselenides*

1.3 Asymmetric Synthesis and the Concept of Asymmetric Counteranion Directed Catalysis

About one and a half centuries ago, the phenomenon of optical activity and chirality were discovered. In 1849, Pasteur was the first person to demonstrate the chirality of molecules, and thirty years later van't Hoff and Le Bel proposed that the four substituents of a carbon atom are situated on the corners of a tetrahedron, which explained perfectly the observation of optical chirality and stereochemistry of natural occurring isomers. The two isomers in Figure 1.2 are image and mirror image, and they are non-superimposable. Molecules which lack an internal plane of symmetry are called enantiomers after the Greek word *enantion* for opposite. The asymmetric carbon atom in the centre of these structures is chiral (*cheir* = hand, due to their relationship like one hand to the other). The characteristic of chiral molecules to interact with circularly polarized light, identified by Pasteur, gives a means to determine the enantiomeric (or optical) purity of a given mixture of enantiomers. It is defined as the quotient of the degree of rotation of the sample compared to that of the enantiomerically pure substance.

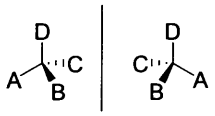


Figure 1.2: *The relationship of enantiomers*

Today, the enantiomeric excess (*e.e.*) of a mixture can also be determined by separation of the enantiomers via HPLC (high pressure liquid chromatography) with chiral columns and integration of the peak areas. The enantiomeric excess is then determined with equation (1), where E^+ is the peak area of the major and E^- is the peak area of the minor enantiomer.

$$e.e. = (E^+ - E^-) / (E^+ + E^-) \qquad (1)$$

If both enantiomers exist in a mixture in equal amounts it is called a racemate or racemic mixture. Since the impact of chiral compounds on living organisms was realized (e.g. Thalidomide scandal), the preparation of enantiomerically pure compounds became a requirement for medicinal chemistry and hence for organic synthesis. Typically, these compounds were accessed either by resolution of a racemate, the use of natures' "natural pool" as starting materials or the use of chiral auxiliaries. A more elegant approach is the generation of pure enantiomers by enantioselective transformations mediated by a chiral reagent.

Generally, three major types of chiral reagents are available for these transformations. The chirality can be induced by either an internal (chiral information is covalently bonded to the reagent) or an

external (the chiral information is introduced via a counterion) source for stereoinformation. The latter case distinguishes between well established anionic processes which are influenced by chiral countercations and the new development of influencing cationic processes by chiral counteranions. The latter concept of Asymmetric Counteranion Directed Catalysis (ACDC) is a relatively new development which emerged in the field of organocatalysis.[6]

1.4 Selenium in Biological Systems

Despite the fact that selenium is commonly classified as toxic, it was found to be an essential trace element in 1957. Selenium in biological systems occurs mainly as selenocysteine (Sec), the selenium analogue of cysteine. Some plants and organisms are able to extract the element from the soil in form of either selenite (SeO_2^{2-}) or selenate (SeO_3^{2-}) and metabolise these species into selenocystein. The selenol moiety in the free amino acid *L*-selenocysteine is very reactive and forms the corresponding diselenides (selenocystin) much faster than the corresponding thiol residues in *L*-cystein disulfides. Beside the occurrence of *L*-selenocysteine in teeth and bones, it is incorporated into enzymes with redox functionalities such as the antioxidant selenoenzyme glutathione peroxidase (GPx), the deiodinating enzyme iodothyronine deiodinase (ID) and the flavin-containing redox enzyme thioredoxin reductase (TrxR). In these enzymes the selenol moiety is mainly deprotonated ($pK_a \sim 5.0$) under *in vivo* conditions due to the higher acidity compared to the thiol ($pK_a \sim 8.6$).

Table 1.2: *Selenocysteine-containing enzymes and their biological functions*[7]

Enzyme	Reaction
Formate dehydrogenases	$HCOOH \rightarrow CO_2 + 2H^+ + 2e^-$
NiFeSe-hydrogenases	$H_2 \rightarrow 2H^+ + 2e^-$
Glycine reductase	$Gly + 2e^- + 4H^+ + ADP + P_i \rightarrow acetate + NH_4^+ + ATP$
Selenophosphate synthetase	$HSe^- + ATP \rightarrow HSe\text{-}PO_3H_2 + AMP + P_i$
Glutathione peroxidases (GPx)	$H_2O_2 + 2GSH \rightarrow H_2O + GSSG$
Phospholipid-hydroperoxide-GPx	$ROOH + 2GSH \rightarrow R\text{-}OH + H_2O + GSSG$
Type I iodothyronine deiodinase	$L\text{-thyroxine} + 2e^- + H^+ \rightarrow 3,5,3'\text{-triiodothyronine} + I^-$
Thioredoxin reductase	$NADPH + Trx_{ox} \rightarrow NADP^+ + Trx_{red}$

An intensively studied enzyme family mentioned in Table 1.2 are the glutathione peroxidases, which are involved in the defence against oxidative stress. The main function of antioxidant GPx selenoenzymes is the reduction of hydroperoxides derived from the lipid metabolism. The selenol functionality (RSeH) in the active site of the enzyme can be oxidised by hydroperoxides to the corresponding selenenic acid (RSeOH), which is then reduced by one equivalent of glutathione

(GSH), forming a selenenylsulfide (RSeSG). Another equivalent of glutathione then reduces the selenenylsulfide (RSeSG) again to the selenol (RSeH) and forms the oxidised form of glutathione (GSSG).

Studies examining the correlation of selenium levels in patients in connection with certain diseases are still ongoing but for example suggest that selenium can have a positive effect, especially when administered together with Vitamin E, to suppress the growing of tumours.[8] In HIV/AIDS patients low selenium levels could be directly correlated with a decreased immune cell count and an increase of the disease progression and the risk of death.[9] Adverse health effects are rather rarely reported, but an increased intake of the element can result in a condition called selenosis and is accompanied by high blood levels of selenium (greater than 100 μg/dl).[10]

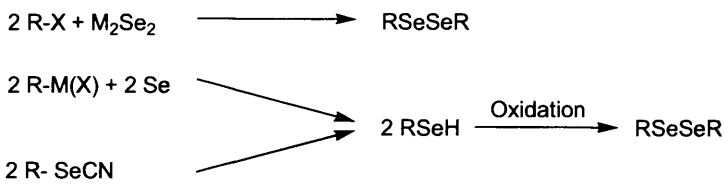
1.5 Aim of This Thesis

The work presented in this thesis is centred on two approaches to synthesise new effective chiral selenenylating reagents. First, the "classical" approach to synthesise these chiral reagents using the inheritant chirality of a selenenyl halide/triflate is detailed. Chapter 2 describes the synthesis of new chiral diselenides, which are used as precursors for successful selenenylation reactions shown in Chapter 3. The influence of solvents, the structural features of styrenes and different nucleophiles are examined. One of the new selenenylating reagents bearing a chiral sulfoxide auxiliary shows an interesting reactivity if the reaction conditions for the selenenylation reaction are altered slightly. These results, including a proposed reaction mechanism, are shown in Chapter 4. Beside this "classical" approach, the concept of counteranion directed catalysis (ACDC) was envisioned as a tool to induce chirality in selenenylation reactions. The results of this quest using different chiral anions together with a range of solvents and selenium electrophiles are presented in Chapter 5. Before this thesis concludes, some results concerning the antioxidant activity of some of the new diselenides as glutathione peroxidase (GPx) mimics will be outlined. Chapter 7 gives a short summary of this work and some perspectives on future developments in this area of research.

2. New Chiral Diselenides

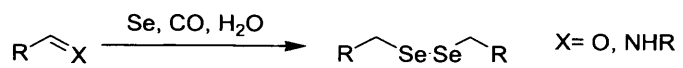
2.1 Overview: Syntheses of Diselenides

There are many different syntheses available for racemic as well as chiral diselenides. However, the synthesis of organoselenium compounds requires the use of elemental selenium at any stage of a reaction sequence. One of the first reliable methods to produce diphenyl diselenide was published in 1979 on a 1 mole scale by Reich,[11] who used the corresponding Grignard reagent as a starting material.



Scheme 2.1: *Synthesis of diselenides*

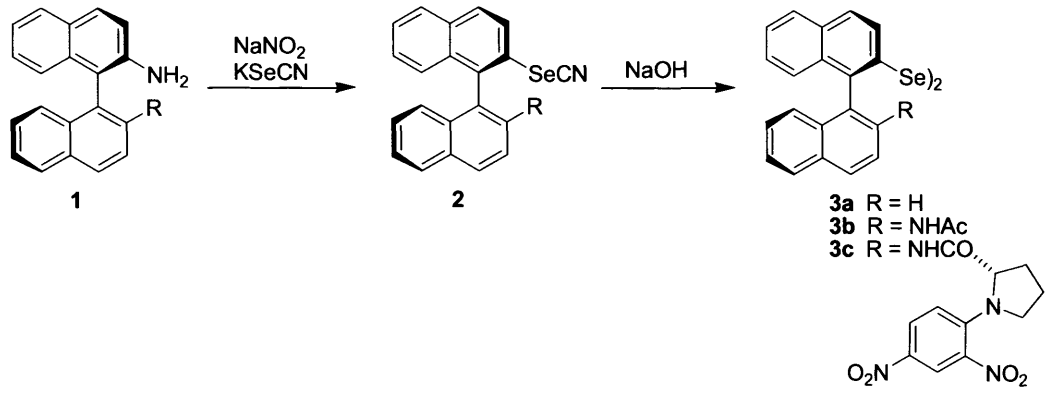
As shown in Scheme 2.1, elemental selenium also reacts directly with other organometallics to produce selenols (RSeH) which can then be oxidised to the corresponding diselenides (RSeSeR). Alternatively, black selenium can be reacted with reducing agents to form selenides (Se^{-}) and diselenides ($^{-}SeSe^{-}$). The most common strategies include the use of alkali metals such as sodium and lithium, in THF with naphthalene[12] or diphenylacetylene[13] as a single electron transfer reagent, samarium diiodide,[14] metal borohydrides,[15] or zinc in the presence of sodium hydroxide.[16] The obtained metal selenide and diselenide intermediates can in turn be subjected to electrophilic organic species and form diorganyl selenides or diorganyl diselenides.



Scheme 2.2: *Synthesis of diselenides from aldehydes or imines*

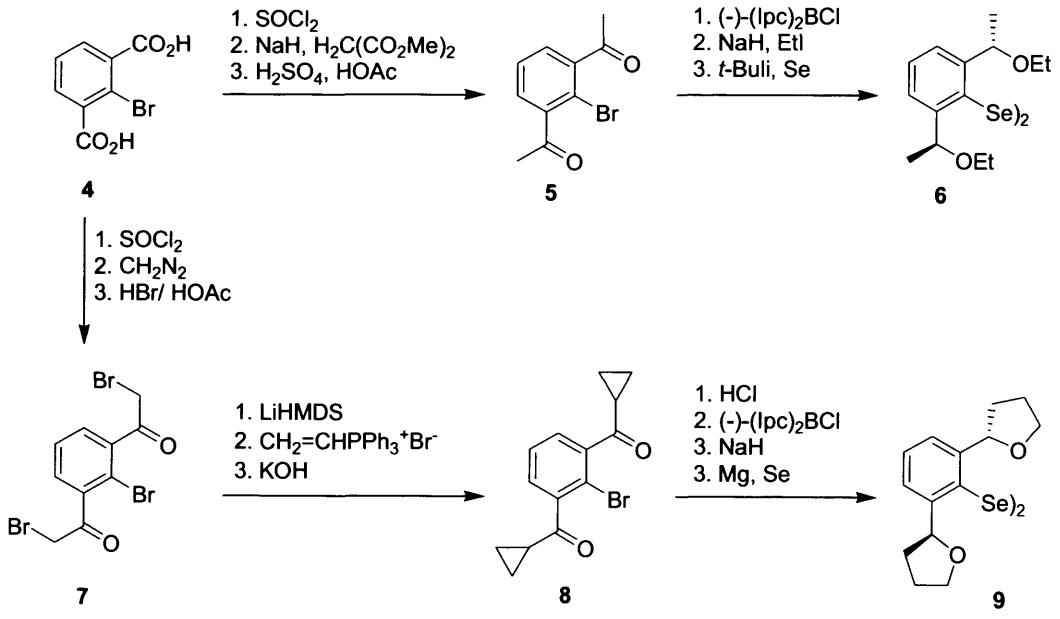
In recent years, some novel procedures were established to prepare these compounds under milder reaction conditions. Diselenides can be prepared reductively from either aldehydes[17] or imines[18] in the presence of carbon monoxide as shown in Scheme 2.2.

In 1988 Tomoda and co-workers synthesised the first chiral diselenides from binaphthylamines[1,19]. The monoprotected chiral binaphthylamines **1** were, after diazotation, treated with potassium selenocyanate and subsequently with aqueous sodium hydroxide. The desired chiral binaphthyl diselenides **3** were obtained in about 30% yield (Scheme 2.3).



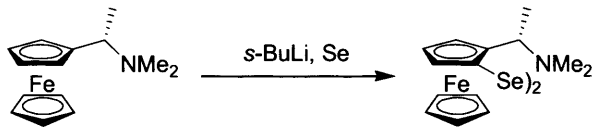
Scheme 2.3: *Chiral binaphthyl - derived diselenides by Tomoda*

At the beginning of the 1990s several new reports of chiral diselenides by Dèziel, Uemura and Tomoda groups were published. Dèziel and co-workers established the two C_2-symmetrical diselenides **6** and **9** which were prepared from 2-bromoisophthalic acid according to Scheme 2.4.[20] The diselenides were obtained in 20% (**6**) and 30% (**9**) overall yield, respectively.



Scheme 2.4: *Dèziel's C_2-symmetrical diselenides*

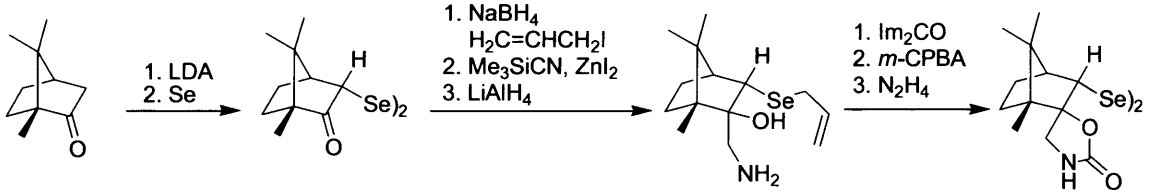
The ferrocenyl skeleton, used by Uemura *et al.* to synthesise chiral diselenides of type **11**, is commercially available but costly.[21] The conversion into the diselenide however was accomplished with 80% yield.



10 **11**

Scheme 2.5: *Chiral ferrocenyl-based diselenides by Uemura*

Camphor-derived chiral diselenides like **13** and **15** were synthesised by Back and co-workers.[22] Diselenide **13** can be prepared from camphor in only one step. Further manipulation is possible after protection of the selenium by allylation. The synthesis of the cyclic carbamate is accomplished via the formation and reduction of the corresponding cyanohydrin compound and subsequent cyclisation (Scheme 2.6). The overall yield of this sequence is 53%.

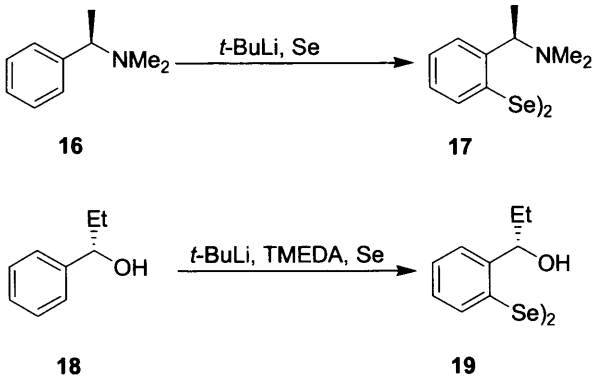


12 **13** **14** **15**

Scheme 2.6: *Chiral camphor-based diselenides by Back*

These selenium electrophiles proved to introduce chirality to various degrees, which led to the idea that more easily accessible and simple chiral diselenides as precursors should also be synthesised. One common starting point in the aforementioned syntheses was the use of diaryl diselenides. The advantages of aryl instead of alkyl derivatives are that the former are easier to handle, they possess increased stability and lower volatility, and their odours are much less offensive than those of the alkyl analogues.

Diselenides such as **17** and **19** were synthesised by Wirth and co-workers[23] in one step from commercially available chiral aromatic precursors via *ortho*-lithiation and addition of elemental selenium (Scheme 2.7). After oxidative work-up, the corresponding diselenides were obtained in yields ranging from 60% to 80%. Another non-racemic analogue of Wirth's diselenides containing sulfur as a hetereoatom instead of oxygen/nitrogen was synthesised by Tiecco and co-workers.[24]



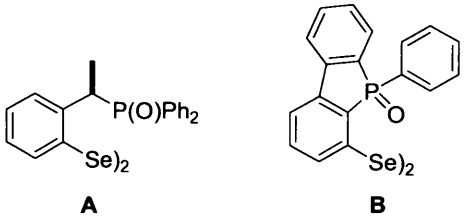
Scheme 2.7: *Chiral diselenides by Wirth*

2.2 Syntheses of New Chiral Diselenides

As mentioned above, diaryl diselenides have certain advantages over the alkyl analogues and it is well known by now that a heteroatom in close proximity to the electrophilic selenium moiety, which can be generated from the diselenide, coordinates to the selenium.[25] The aim of this part of the work was to synthesise new aromatic diselenides with chiral phosphorous or sulfoxide centres in coordinative distance to the selenium as precursors for new chiral selenenylating reagents.

2.2.1 Phosphorous Oxides as Coordinating Moieties to Selenium and as Centre of Chirality

Phosphine oxides are considered the most stable of the organophosphorous compounds, with triphenylphosphine oxide decomposing only above 450 °C. A study by Chesnut suggests that the PO bond in phosphine oxides is a highly polarised σ-bond with strong back bonding of the oxygen π-orbitals.[26] Although the strong PO bond is well symbolised by the formula $R_3P{=}O$, according to Chesnut's findings it seems to be more accurate to depict it as $R_3P^{+}{-}O^{-}$. The strong, polar and short bond of phosphine oxides makes these moieties very interesting coordinating auxiliaries in selenenylating reagents.

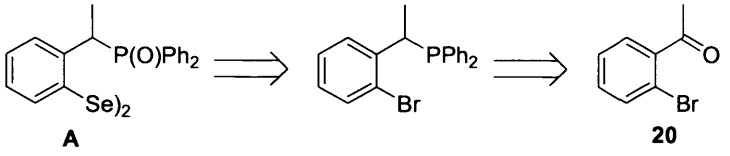


Scheme 2.8: *Proposed phosphorus-containing diselenides*

Until now there are no phosphorous containing diselenides known where phosphorous oxides are used as coordinating heteroatoms or as chiral centres to control the stereoselective outcome of selenium

electrophile mediated reactions. The task was therefore to synthesise compounds with either a phosphorous/oxygen moiety with oxygen as coordinating heteroatom to the selenium (type A) or phosphorous as the chiral centre with oxygen as the coordinating atom (type B) (Scheme 2.8).

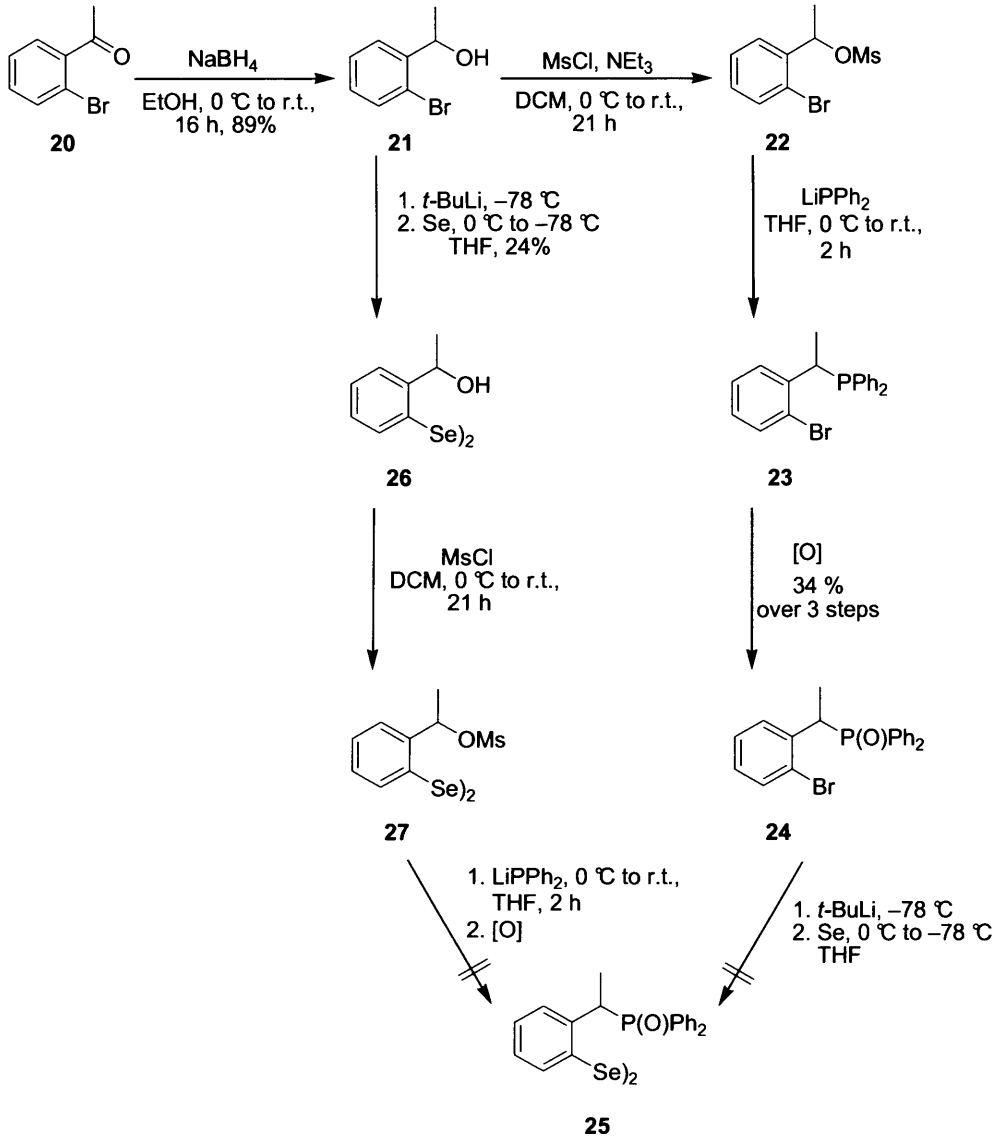
In the beginning a racemic route for the synthesis of compounds **A** and **B** was followed. The ability of their corresponding selenium electrophiles to induce diastereoselectivity in selenenylation reactions can be determined even with the racemic precursors (see Chapter 3.1). Following the previous successful syntheses of diselenides **17** and **19** by the Wirth group, 2'-bromoacetophenone **20** was chosen as the starting material for the synthesis of racemic diselenides of type **A** (Scheme 2.9).



Scheme 2.9: *Retrosynthesis for phosphorus containing diselenides of type A*

Commercially available ketone **20** was reduced with sodium borohydride in ethanol to afford 1-(2-bromophenyl)ethanol **21** in 89% yield (Scheme 2.10).[27] Through an appropriate reduction with either (+)–DIP-Cl or (–)-DIP-Cl [(–)-Diisopinocampheyl chloroborane] this step could be performed in a stereoselective manner. 1-(2-Bromophenyl)ethanol **21** was planned to be tosylated for further transformation to phosphine **23**. Thus **21** was treated at 0 °C with either *p*-TsCl (4-toluenesulfonyl chloride) in pyridine[28] or *p*-TsCl and DMAP (4-dimethylaminopyridine) in dichloromethane.[29] The formation of the tosylated alcohol required stirring for more than 24 hours and the resulting tosylate seemed to be very unstable. To circumvent these problems alcohol **21** was mesylated with methanesulfonyl chloride in presence of triethylamine in dichloromethane.[30] After 24 hours, a complete conversion was observed but, like the tosylate, the mesylate was extremely unstable. However, a crude NMR spectrum of the mesylated product **22** proved its formation. Due to the fact that the tosylation needs more time than the mesylation, the subsequent reaction was performed with the mesylate. The decomposition of the mesylate could be avoided by a one pot synthesis of phosphine **23**. A solution of **22** was treated at 0 °C with lithium diphenylphosphine, which was obtained from the reaction of diphenylphosphine with *n*-butyllithium at 0 °C in dry THF after stirring for 30 min.[31] However, this approach resulted in a complex reaction mixture. After a fast workup of the mesylate **22** and immediate reaction of the crude product, redissolved in THF, with lithium diphenylphosphine at 0 °C, the product (**23**) could be obtained. Due to the high reactivity of phosphine **23** it was oxidised to the phosphine oxide **24** during column chromatography. The following reaction with *t*-butyllithium and selenium resulted in a complex mixture, which did not contain the expected product. The phosphine oxide seemed to undergo lithium exchange reactions with *t*-butyllithium which led to various undefined products. To circumvent this problem, 1-(2-bromophenyl)ethanol **21** was reacted

with *t*-butyllithium and selenium to give the diselenide **26** in 24% yield. Further 25% could be identified as a mixture of the corresponding mono- and triselenides and 50% as 1-phenylethanol. The subsequent mesylation was followed by TLC. After complete consumption of the starting material the mixture was subjected to a fast workup and immediately used for the next reaction. The reaction of **27** with $LiPPh_2$ was again carried out at –78 °C in THF, but resulted, again, in a complex mixture.



Scheme 2.10: *Planned route to phosphorus containing diselenide **25***

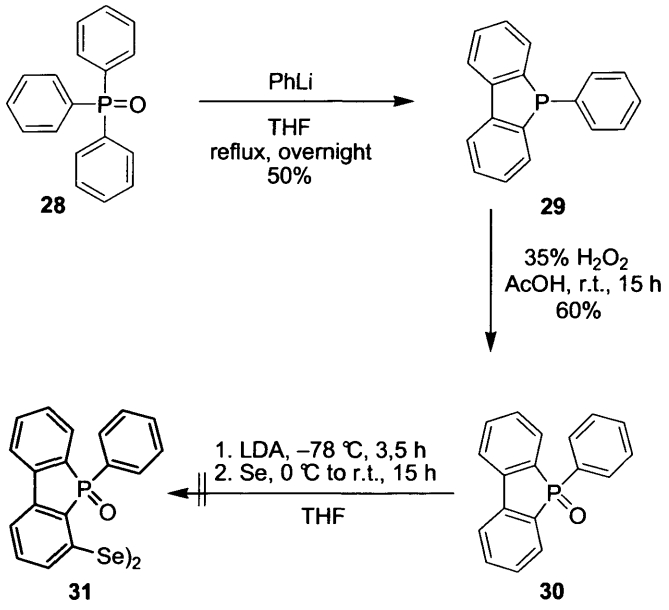
Another possibility to synthesise diselenide **25** could be to follow the first route and the introduction of selenium in the last step via the formation of the Grignard reagent of compound **24**. However, as there is a general possibility that the selenium can react with the phosphorus atom in the molecule, this idea was not investigated further.

The second envisioned phosphorus compound of type **B** (Scheme 2.8) was planned to be synthesised in three steps from triphenylphosphine oxide **28** (Scheme 2.11). Furukawa *et al.*[32] described a simple

preparation of (2,2′-biphenylylene)-phenylphosphine oxide **30**. When treated with LDA, lithiation took place regiospecifically at the 3-position in the biphenyl ring.

Thus, triphenylphosphine oxide **28** was treated with phenyllithium and refluxed for 12 hours to yield (2,2′-biphenylylene)phenylphosphine **29** in 50% yield. The reaction was also performed with triphenylphosphine according to a procedure published by Widhalm *et al.*,[33] but the product could only be found in traces. (2,2′-Biphenylylene)phenylphosphine **29** was then oxidised to the corresponding phosphine oxide **30** in 60% yield. Lithiation and addition of selenium to phosphine oxide **30** afforded a complex product mixture. Mass spectroscopy indicated the formation of an ion with the appropriate mass but the product could not be isolated after chromatography.

As both attempts to synthesise phosphorus containing diselenides failed, further attempts to synthesise these compounds were deferred.

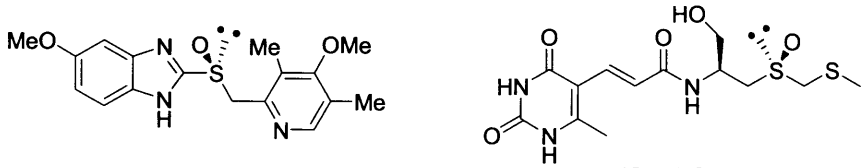


Scheme 2.11: *Planned route to phosphorus-containing diselenide **31***

2.2.2 Sulfoxides as Chiral Auxiliaries

Another heteroatom with the potential use as a chiral auxiliary in diselenides is sulfur in its sulfoxide oxidation stage. Sulfoxides are represented by the structural formula R-S(=O)-R'. The sulfur-oxygen bond in these compounds has, in contrast to the keto analogues, a significantly stronger dipole moment with the negative charge centred on the oxygen atom. The bonding in sulfoxides is similar to that found in tertiary phosphine oxides, $R_3P{=}O$, as described previously (Chapter 2.2.1). The geometry on the sulfur atom in the sulfoxide oxidation state is tetrahedral due to the lone electron pair on the sulfur, leading to large stereoelectronic differences and a geometry similar to sp^3-hybridised carbons.[34]

Hence, these compounds allow the creation of a well-defined chiral environment around the sulfur atom. If the two organic substituents are different, the sulfur is a chiral centre and the energy required for the inversion is sufficiently high that the stereocentre is stable even at higher temperatures. In general, the thermal stereomutation of sulfoxides occurs at a significant rate only at about 200 °C, as indicated by the values of the activation parameters of the pyramidal inversion determined for various sulfoxides [from 35 to 42 kcal/mol for $\Delta H^{\#}$, and from –8 to +4 cal/(mol K) for $\Delta S^{\#}$].[35] Benzyl and allyl sulfoxides, which racemise at lower temperatures (130–150 °C and 50–70 °C, respectively), are exceptions from this rule. Chiral sulfoxides can find applications in certain drugs such as (*S*)-Esomeprazole and (S,R_S)-Sparsomycin (Scheme 2.12), and they can also be employed as chiral auxiliaries.

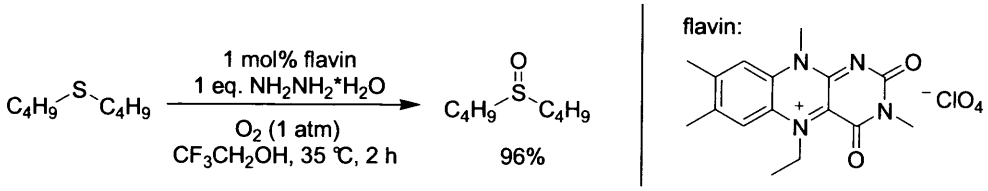


(*S*)-Esomeprazole (S,R_S)-Sparsomycin

Scheme 2.12: *Structures of (S)-Esomeprazole and (S,R$_S$)-Sparsomycin*

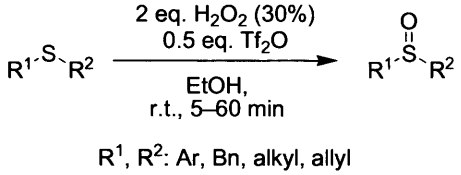
Racemic sulfoxides can be synthesised by simple oxidation of sulfides with numerous oxidative reagents. Periodates or peroxides are most commonly employed in these reactions. Leonard and Johnson were the first to report the use of sodium periodate as oxidant for sulfides to obtain sulfoxides free from sulfide or sulfone.[36] The procedure is easily employed and affords the desired products in 62% to 99%. A recent example for the selective oxidation of sulfides to sulfoxides with periodic acid (H_5IO_6) was reported by Kim and co-workers.[37] The experimentally simple sulfoxidation is catalysed by $FeCl_3$ in acetonitrile with good reported yields. The reaction times were often less than 2 minutes.

Various organic substrates such as amines and sulfides can also be oxidised with molecular oxygen (1 atm) in the presence of 5-ethyl-3-methyllumiflavinium perchlorate as catalyst, hydrazine monohydrate and 2,2,2-trifluoroethanol as solvent (Scheme 2.13).[38]



Scheme 2.13: *Sulfoxidation procedure by Murahashi*[37]

Khodaei *et al.* found a procedure to oxidise sulfanes to sulfoxides with a combination of hydrogen peroxide and triflic anhydride.[39] Their method avoids over-oxidation and tolerates sensitive functional groups (Scheme 2.14).



Scheme 2.14: *Sulfoxidation procedure by Khodaei*[38]

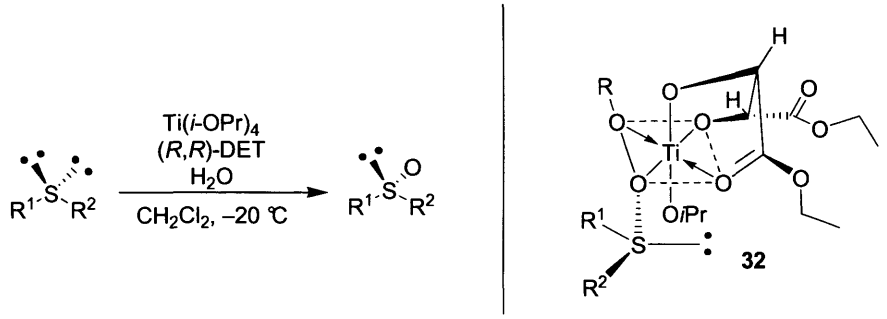
Another sulfoxidation of alkyl-aryl sulfides used $Sc(OTf)_3$ and hydrogen peroxide as an efficient catalyst system.[40] According to the authors, common protecting groups are compatible with this methodology and over-oxidation is kept to a minimum.

Chiral non-racemic sulfoxides can be synthesised by various methods with high enantiomeric purity, and there are still new developments in this area of research.[41] The most direct route to chiral non-racemic sulfoxides is the asymmetric oxidation of sulfides, and the use of either steric- or neighbouring-group participation leads to good stereocontrol.[42] Nevertheless, most of the commonly synthesised sulfoxides are unfunctionalised and hence the chiral oxidation is more challenging. A range of enantioselective sulfoxidation methods were therefore developed using chiral oxaziridines or peroxides, as well as biological tools like enzymes and antibodies. Other methods include the asymmetric oxidation of metal-complexed prochiral thioethers and the metal-catalysed enantioselective chemical sulfoxidation. Beside the oxidative methods, there are also very successful syntheses in the literature that use nucleophilic substitution on pure chiral sulfur derivatives to produce enantiomerically pure sulfoxides. These methods rely on either enantiomerically pure or diastereomerically pure chiral sulfur derivatives. A comprehensive review on this topic was published by Fernández and Khiar.[40f] The most commonly employed strategies from the list above, however, are the metal-catalysed enantioselective chemical sulfoxidation and the nucleophilic substitution on diastereomerically pure chiral sulfur derivatives.

The metal-catalysed enantioselective sulfoxidation employs different C_2-symmetric diols as ligands to titanium, C_3-symmetric aminotriol-titanium complexes or metal-salen complexes (Mn, V, Ti). In the following paragraphs a short outline of these oxidative methods is given.

Based on Sharpless' epoxidation method for the asymmetric epoxidation alkenes, using 5–10 mol% Ti(*i*-OPr)$_4$, (+)- or (–)-diethyltartrate, *t*-butyl hydroperoxide (TBHP) (1:1:2) and activated molecular sieves in dichloromethane at –20 °C,[43] Kagan found that by addition of one mole equivalent of water the reagent mixture was able to stereoselectively oxidise prochiral sulfides to sulfoxides (Scheme 2.15).[44] After improvement of the catalytic procedure, it was determined that the combination

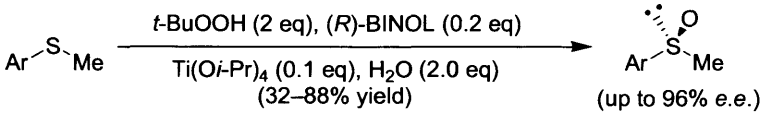
Ti(*i*-OPr)$_4$/(*R*,*R*)-diethyltartrate/*i*PrOH (1:4:4) and cumene hydroperoxide in the presence of 4 Å molecular sieves are the optimal conditions to achieve high enantioselectivity.[45]



Scheme 2.15: *Ti-mediated chiral oxidation of sulfides by Kagan*

Kagan originally proposed the formation of a dimer of two titanium atoms which are connected via an η-oxo bridge, but as shown in Scheme 2.15 with the new system, using *i*-propanol, the complex **32** bears a simple *iso*-propoxide ligand. The approach of the incoming sulfide is determined by an efficient distinction between the larger (R^1) and the smaller (R^2) substituent at the sulfur atom and the system furnishes chiral sulfoxides with very high *e.e.* (75–95%). Similar results were obtained by the group of Modena who used a 1:1:4 ratio of *t*-butyl hydroperoxide (TBHP)/Ti(O*i*-Pr)$_4$/(*R*,*R*)-DET at –20 °C in toluene or 1,2-dichloroethane.[46]

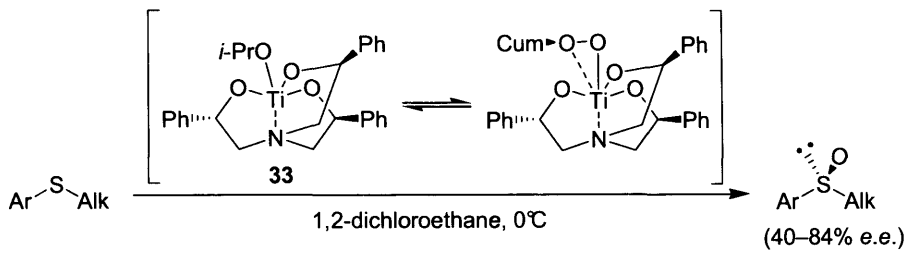
Uemura improved the catalytic asymmetric oxidation of prochiral sulfides using Ti(O*i*-Pr)$_4$ in the presence of (*R*)-(+)-binaphthol (Scheme 2.16).[47] The highest *e.e.* was obtained with TBHP at 25 °C, with 5 mol% of the chiral ligand leading to sulfoxides with (*R*)- or (*S*)- absolute configuration, and up to 96% *e.e.*



Scheme 2.16: *Ti-mediated chiral oxidation of sulfides by Uemura*

Several other groups also developed similar effective chiral Ti(IV) catalysts, using different C_2-symmetric diols with variable steric and stereoelectronic features.[48]

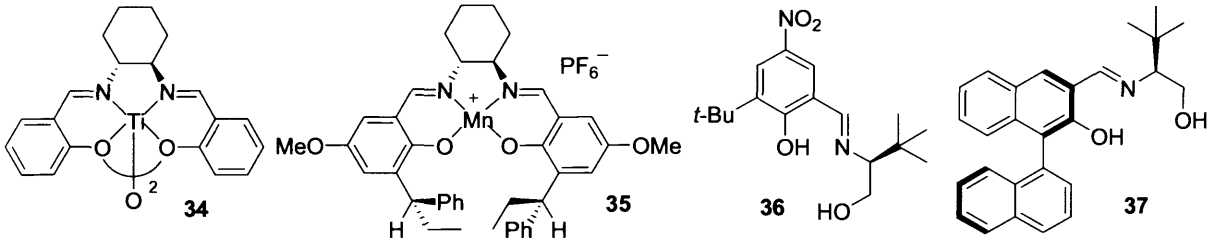
Licini and Nugent used a C_3-symmetric chiral trialkanolamine ligand for the oxidation of aryl alkyl sulfides (Scheme 2.17).[49] The reactions were performed with cumyl hydroperoxide (CHP) in the presence of 1–2% catalyst **33** and resulted in enantiomeric excesses in the range of 40–84%. However, the optical purities of the final sulfoxides were shown to be in part due to kinetic resolution.



Scheme 2.17: *Ti-mediated chiral oxidation of sulfides by Licini and Nugen*

Fujita developed a binuclear Schiff base-titanium(IV) complex **34** (Scheme 2.18), which catalyses the asymmetric oxidation of methyl phenyl sulfide with only 4 mol% catalyst and trityl hydroperoxides in methanol at 0 °C. The (*R*)-methyl phenyl sulfoxide was obtained with 60% *e.e.*[50] A (salen)-manganese(III) complex **35** (Scheme 2.18), reported by Katsuki, showed also good catalytic asymmetric induction in the oxidation of sulfides (up to 90% *e.e.*) using PhIO as terminal oxidant.[51]

Another system, developed by Bolm, is formed *in situ* from $VO(acac)_2$ and ligand **36** (Scheme 2.18).[52] This system is able to catalyse the oxidation of aryl alkyl sulfides under simple reaction conditions, using 30% aqueous H_2O_2 as the terminal oxidant and with simple ligands derived from (*S*)-*t*-leucinol. The sulfoxidation is usually conducted using the catalyst formed *in situ* from 1 mol% of $VO(acac)_2$ and 1.5 mol% of imine and gives *e.e.*'s up to 70%. Some time ago, Berkessel found that ligand **37** (Scheme 2.18) shows even better results in the $H_2O_2/VO(acac)_2$-mediated oxidation of thioanisole (92% yield and 78% *e.e.*) than Bolm's system (73% yield and 59% *e.e.*).[53]

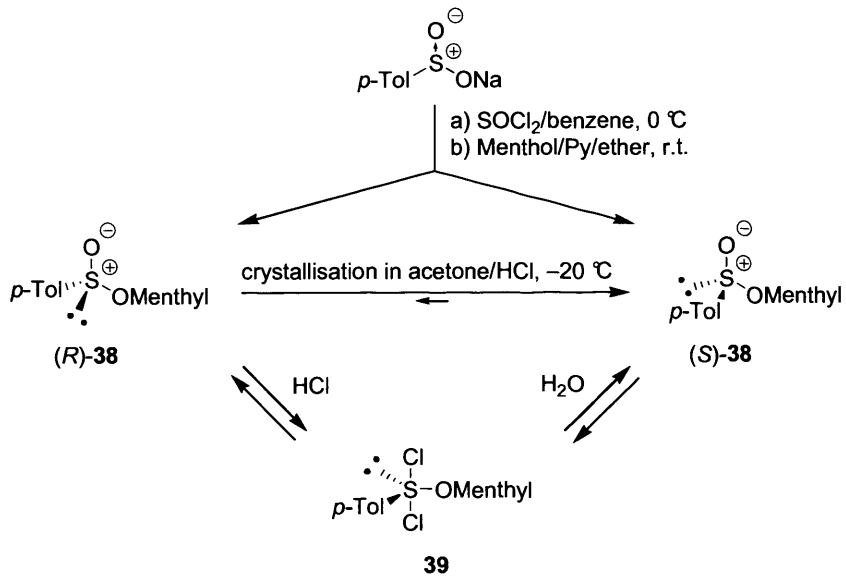


Fujita Katsuki Bolm Berkessel

Scheme 2.18: *Chiral metal-salen complexes for the oxidation of sulfides*

Besides the direct sulfoxidation methods described above, there is also the possibility to employ nucleophilic substitution reactions on diastereomerically pure chiral sulfur derivatives. For this approach, the synthesis of a sulfinylating agent with an electrophilic sulfur of known configuration is necessary. After this preliminary step the chiral sulfoxide is released by nucleophilic addition of a metal-organic reagent. The sulfinating agent can either be a cyclic reagent or a diastereomerically pure acyclic compound. The most widely employed method, using diastereomerically pure acyclic sulfinylating reagents, depends on either a good kinetic resolution or a high separation factor of the

intermediate diastereomers. At the beginning of the 1960s, Andersen proved that nucleophilic substitution of diastereomerically pure (–)-(*S*)-menthyl sulfinates with Grignard reagents leads to enantiopure sulfoxides with high yields.[54]



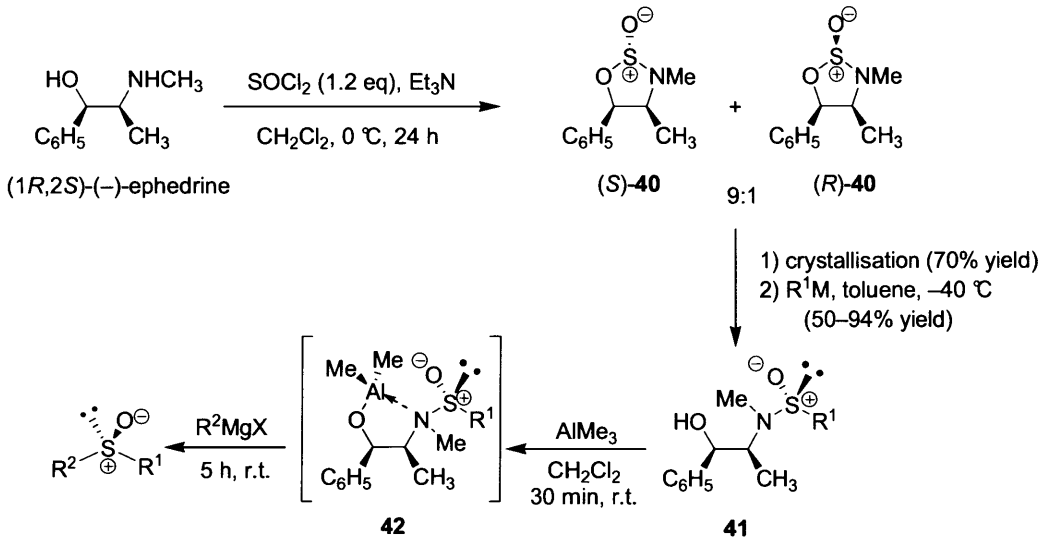
Scheme 2.19: *Epimerisation of sulfinate esters shown by Mioskowski and Solladié*[54a]

Additionally, Mioskowski and Solladié could show that crystallisation in acidic medium led to the epimerisation of sulfinate esters (*R*)-**38** and (*S*)-**38** (Scheme 2.19). The epimerisation occurred through the achiral intermediate **39**[55] allowing the less soluble isomer (*S*)-**38** to be obtained in very high yield (80–90%).[56] Although these methodologies allow the synthesis of a wide variety of enantiomerically pure aryl sulfoxides, enantiopure dialkyl sulfoxides cannot be obtained by these methods. This problem led in the early 1990s to the development of new methodologies especially of diastereomerically pure cyclic sulfinylating transfer reagents.

Two different cyclic reagents were developed for this purpose, the aminosulfite methodology and the sulfite methodology. Both follow a similar three-step procedure which starts with the formation of a chiral cyclic aminosulfite or a cyclic sulfite. These compounds are then ring opened by two consecutive reactions with organometallic reagents to afford a chiral sulfoxide.

In 1973, the first use of a cyclic aminosulfide as chiral auxiliary (ephedrine) was developed by Wudl and Lee (Scheme 2.20).[57] Upon reaction of ephedrine with thionyl chloride at 0 °C and triethylamine as base, it was possible to isolate 1,2,3-oxathiazolidine-*S*-oxides (aminosulfites) **40** in good yields after recrystallisation, although only with moderate selectivity (44% *d.e.*). Wudl and Lee also found that the first organometallic reagent reacted chemoselectively with the aminosulfide function and that the second substitution only occurred with organolithium reagents. This unfortunately also led to some significant racemisation. Therefore the procedure was modified by Snyder and Benson.[58] It was

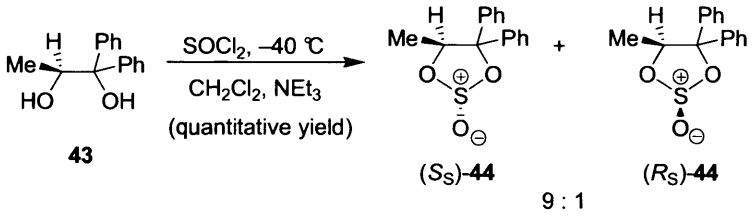
possible to obtain the sulfoxides in high yield after storage of the diastereomers at 0 °C for 24 h in the presence of $Et_3N{\cdot}HCl$, with a diastereoselectivity of up to 80% after recrystallisation.



Scheme 2.20: *Nucleophilic substitution on chiral, diastereomerically pure cyclic aminosulfites*

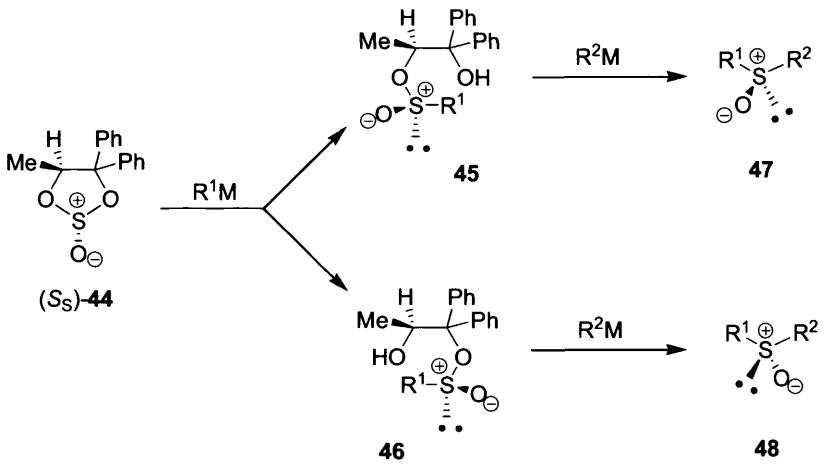
A major drawback of these reactions was that neither phenyl organometallic reagents nor *t*-butyl Grignard reagents were able to give the corresponding intermediate sulfinamides **41** in good yields. Additionally, it was nessessary to add $AlMe_3$ to the intermediate sulfinamide **42** prior to the addition of the Grignard reagent.

To avoid some of the problems encountered by the previous methods, Kagan reported the use of a five-membered ring cyclic sulfite **44**.[59] This sulfite could be prepared by the use of a chiral diol **43**, which can be obtained from *L*-ethyl lactate in one step (75%) as highlighted in Scheme 2.21.[60]



Scheme 2.21: *Synthesis of diastereomerically pure cyclic sulfites by Kagan*

The reaction of **43** with $SOCl_2$ led to a 1:1 mixture under standard conditions. However, Kagan could obtain a 9:1 mixture of *trans*- and *cis*-sulfite, (S_S)-**44** and (R_S)-**44** after a change in reaction conditions. Slow addition of triethylamine to a solution of diol **43** and thionyl chloride in CH_2Cl_2 at –40 °C led to the preferred formation of sulfite (S_S)-**44** which was isolated in 70% yield after crystallisation from hexane.



Scheme 2.22: *Synthesis of enantiomerically pure sulfoxides by Kagan*

Chiral sulfite (S_S)-**44** reacts cleanly with a range of organometallic reagents to give the corresponding intermediate sulfinate esters **45** or **46** (Scheme 2.22). An X-ray analysis of (S_S)-**44** confirmed its absolute stereochemistry, which was already assumed as sulfoxides **47** and **48** would be released after a double inversion of configuration in both successive reactions with organometallics R^1M and R^2M. Interestingly, Kagan was also able to show that the regioselectivity in the first ring-opening step of the cyclic sulfite (S_S)-**44**, with two potential leaving groups, is closely related to the steric volume of the organometallic used (Table 2.1).

Table 2.1 *Synthesis of chiral sulfinates **45** and **46** from sulfite (S_S)-**44***

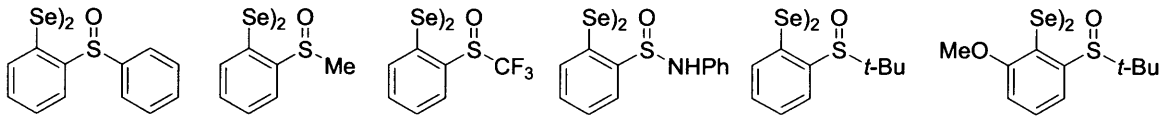
Entry	R^1M	45:46	Yield[a] of major sulfinate (%)
1	MeLi	25:75	55
2	MeMgI	20:80	70
3	EtMgBr	9:91	80
4	*n*-OctMgBr	5:95	60
5	*t*-BuMgBr	95:5	60
6	*t*-BuMgCl	90:10	70
7	*t*-BuLi	[b]	
8	BnMgCl	30:70	50
9	BnMgBr	45:55	[c]
10	HC=CHMgCl	5:95	50
11	MesitylMgBr	88:12	70
12	PhMgBr	50:50	[c]

(a) Purification by crystallisation. (b) Only di-*t*-butyl sulfoxide is obtained. (c) Separation of the two diastereomers by crystallisation failed.

As is shown in Table 2.1, when R^1 is small (ethyl, *n*-octyl or vinyl), sulfinate **46** is the major product and can be obtained in up to 80% yield. In contrast, if R^1 is a bulky substituent, such as *t*-butyl or mesityl, the isomer **45** is mainly obtained in yields up to 70%. Only moderate selectivity was observed with MeLi (75:25) and very poor selectivity in the cases of benzyl and phenyl sulfinates. After recrystallisation, the optically pure sulfinates **45** and **46** were smoothly transformed to the corresponding optically pure sulfoxides. Various dialkyl, alkyl aryl, and diaryl sulfoxides have been synthesised with a distereomerically pure sulfinate and 2 equivalents of the Grignard or organolithium reagent in THF at room temperature in quantitative yield and with up to 100% *e.e.* Both enantiomers of the sulfoxides are accessible from the same chiral cyclic sulfite by inversion of the addition of the organometallic reagents if only two small or two bulky substituents are used. In other cases the use of commercially available (*R*)-*i*-butyl lactate as starting material would lead to the desired isomeric sulfoxide. Although Kagans methodology is time-consuming, it gives easy access to chiral *t*-butyl sulfoxides, which was still a challenge with the methods described previously.

2.2.3 Synthesis of Racemic Diselenides with Sulfoxides as Centre of Chirality

The synthesis of several sulfoxide-containing aromatic diselenides shown in Scheme 2.23 was envisioned. In the beginning, it was planned to prepare these diselenides as racemic mixtures to establish the general feasibility to produce these structures from commercially available starting materials in a few steps.



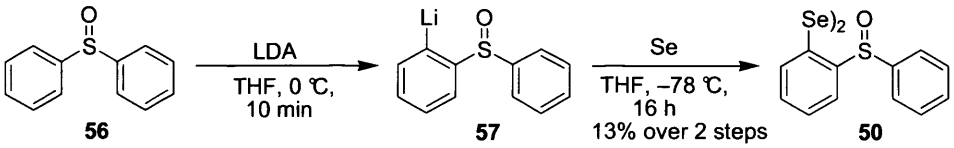
50 **51** **52** **53** **54** **55**

Scheme 2.23: *Envisioned new sulfoxide-containing aromatic diselenides*

In all cases the introduction of the selenium could be realised by *ortho*-lithiation of the sulfoxides and subsequent addition of elemental selenium to produce the corresponding selenols. As mentioned in Chapter 2.1, the obtained selenols are readily oxidised with air to the corresponding diselenides.

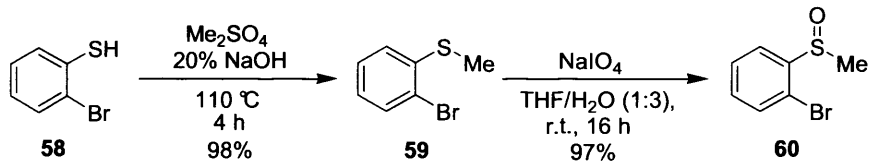
Diselenide **50** was synthesised from commercially available diphenyl sulfoxide **56** via *ortho*-lithiation with LDA in THF at –78 °C (Scheme 2.24).[61] This solution was treated with elemental selenium and stirred overnight at room temperature. Then the mixture was quenched with 1M hydrochloric acid and extracted with diethyl ether. The combined ether extracts were treated with potassium hydroxide pellets to facilitate the oxidation of the selenol to the diselenide and then dried with sodium sulfate. A

mixture of starting material and tri- and diselenides was obtained. It was possible to separate the triselenide products from the diselenides by column chromatography. Diselenide **50** was obtained in 13% yield.



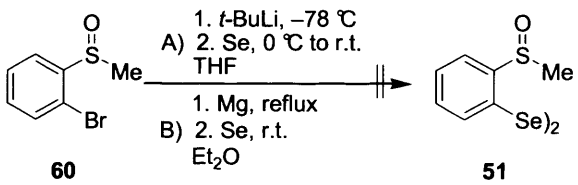
Scheme 2.24: *Route to sulfoxide containing diselenide* ***50***

For the synthesis of diselenide **51** the corresponding 2-bromophenylmethyl sulfoxide **60** was chosen as starting material, which should allow the incorporation of selenium after bromine-lithium exchange with *t*-butyllithium. First, **60** was prepared from **58** in two steps (Scheme 2.25). 2-Bromothiophenol was methylated with dimethyl sulfate in the presence of sodium hydroxide under reflux.[29] 2-Bromothioanisole **59** could be isolated in 98% yield and was then oxidised to the corresponding sulfoxide with sodium periodate in a 1:3 water/THF mixture at room temperature.[35] This reaction afforded sulfoxide **60** in 97% yield without any over-oxidised sulfone side product.



Scheme 2.25: *Synthesis of 2-bromophenyl methyl sulfoxide* ***60***

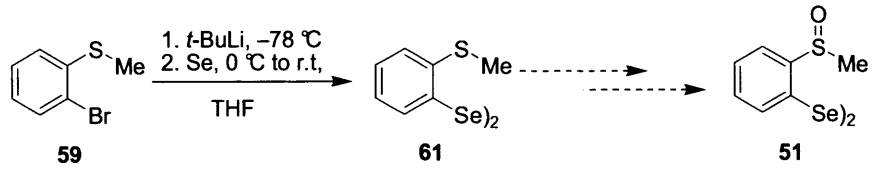
As shown in Scheme 2.26, the conversion to the diselenide **51** was initially attempted with *t*-butyllithium in THF (path A). This reaction produced a complex mixture of products due to several occurring side reactions. First, the very fast sulfur-lithium exchange at the sulfoxide oxidation stage leads to a displacement of the sulfoxide through treatment with organolithium species.[62] Second, the acidity of the methyl protons (pK_a = 33 in DMSO) is much higher compared to the aromatic protons (benzene, pK_a = 43 in DMSO).[63]



Scheme 2.26: *Attempted syntheses of diselenide* ***51***

Although the reactivity of Grignard reagents towards aromatic sulfoxides is similar to that of lithium organyls, it was attempted to generate the Grignard compound *in situ* to accomplish the product formation (Scheme 2.26, path B). Therefore, sulfoxide **60** was reacted with magnesium in diethylether.[64] However, it seemed that the formation of the Grignard reagent is rather slow compared to the reactivity of the already formed Grignard reagent towards the sulfoxide. Hence this route also resulted in a displacement of the sulfoxide prior to the addition of selenium.

Another possibility to obtain the desired diselenide **51** would be to prepare diselenide **61** from 2-bromothioanisol **59** first (pK_a of CH_3 = 42 in DMSO),[62] and to then oxidise sulfide **61** to the sulfoxide **51** (Scheme 2.27).

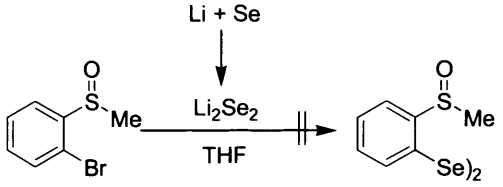


59 **61** **51**

Scheme 2.27: *Synthesis of 2-(methylthio)phenyl diselenide **61***

As the diselenide functionality would be oxidised first due to its higher reactivity, it would be necessary to reduce the selenium moiety back to the selenol in the presence of the sulfoxide. Otherwise the selenium would need to be protected e.g. by bromination[65] to permit the oxidation of the sulfur atom in the presence of selenium. Nevertheless, 2-bromothioanisol **59** was treated with *t*-butyllithium and selenium in THF. Unfortunately, this led only to traces of 2-(methylthio)phenyl diselenide **61** which could not be isolated as a pure compound.

In a last attempt the synthesis of diselenide **51** was to be accomplished by treatment of bromide **60** with dilithium diselenide in THF at room temperature (Scheme 2.28). This procedure would have the advantage that the previous observed reactivity would be suppressed. Dilithium diselenide can be obtained from equimolar amounts of lithium and selenium with catalytic amounts of diphenylacetylene in THF by stirring at room temperature.[12]

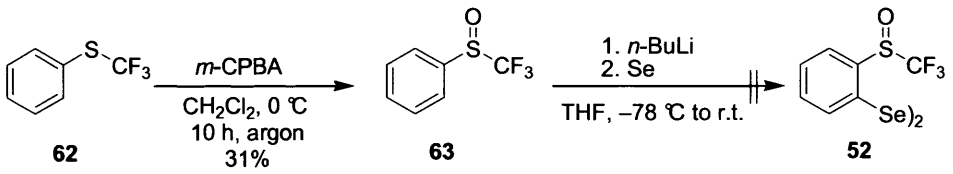


60 **51**

Scheme 2.28: *Attempted synthesis of diselenide **51***

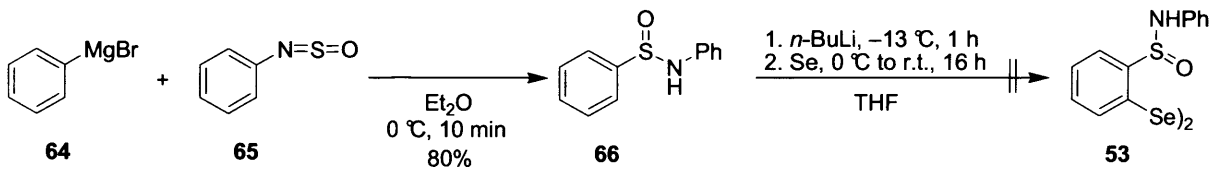
However, it was not possible to isolate diselenide **51** after aqueous workup. The reason for the failure of this reaction is not obvious, as the success of this reaction depends on two factors, firstly the formation and quality of the dilithium diselenide and secondly on the reactivity of bromide **60**. It cannot be ruled out that reactivity of the bromide is sufficient for the conversion to the diselenide. In this case, the formation (or quality) of the dilithium diselenide would be the major problem. Although dilithium diselenide could have been substituted with disodium diselenide to test this hypothesis, further attempts for the synthesis of diselenide **51** were deferred.

Instead it was attempted to produce diselenide **52**, which would be a close analogue of **51**, but with the advantage that an *ortho*-lithiation on the aromatic ring system should be possible (Scheme 2.29). The commercially available sulfide **62** could not be oxidised with sodium periodate in THF/water, which were the identical conditions used for the oxidation of 2-bromomethylphenyl sulfide **59**. Presumably, due to the strong electron withdrawing effect of the three fluorine atoms. An effective method for the oxidation of **62** should be a procedure by Shreeve, Yang and Kirchmeier who achieved 91% yield employing *m*-CPBA as oxidant (Scheme 2.29).[66] However, **63** could only be isolated in 31% yield.



Scheme 2.29: *Attempted synthesis of diselenide 52*

The following reaction of sulfoxide **63** with *n*-butyllithium and elemental selenium proved again the substantial electronic difference of the fluoromethyl compared to the methyl groups, which prevented the *ortho*-lithiation on the aromatic ring system. In theory, the lithiation and subsequent introduction of selenium could be accomplished with a 2-halogen substituted sulfoxide compound analogue to **63**. In this case the synthesis could be realised with 2-bromothiophenol **58** as starting material. After introduction of the trifluoromethyl group[67] and subsequent oxidation, the synthesis of the diselenide should be able to proceed. Unfortunately, due to a lack of time, it was not possible to follow up this route.



Scheme 2.30: *Attempted synthesis of sulfonamide diselenide 53*

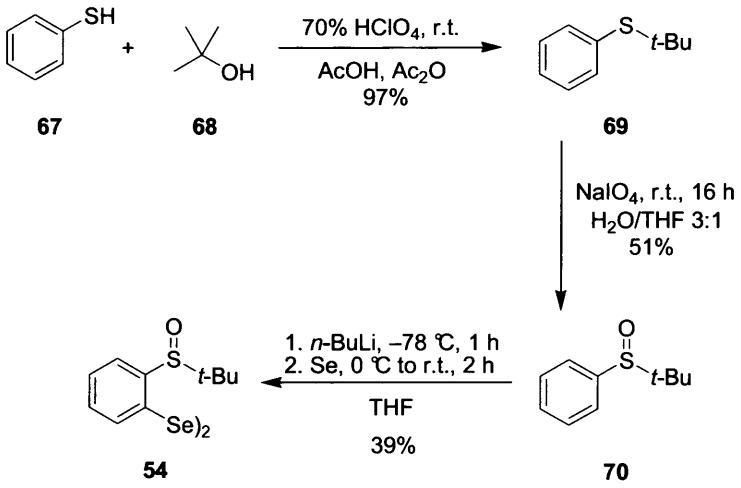
In an early stage of this work, it was also tried to use sulfinamides as chiral auxiliaries (Scheme 2.30). Hence, *N*-phenylbenzenesulfinamide **66** was synthesised from phenylmagnesium bromide **64** and *N*-

thionylanilin **65** in diethylether at 0 °C. After 10 min *N*-phenylbenzenesulfinamide **66** was obtained in 84% yield.[68] The following *ortho*-lithiation[69] and addition of selenium afforded a complex product mixture from which the desired diselenide **53** could not be isolated.

The failure of the synthesis of diselenide **51** was caused by the more acidic methyl protons which prevented an *ortho*-lithiation strategy on the aromatic ring system. This led to the idea that the substitution of the methyl group with a *t*-butyl group could lead a more successful precursor for the introduction of selenium.

According to a publication by Metzner and co-workers[61] it is indeed possible to successfully *ortho*-lithiate *t*-butylphenyl sulfoxide. Hence the synthesis of diselenide **54**, bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, was attempted. Diselenide **54** should be synthesised from the corresponding sulfide **69**, after oxidation to sulfoxide **70**. Sulfide **69** was synthesised from thiophenol **67** and *t*-butanol **68**. According to Katritzky *et al.*, this reaction should occur with concentrated sulfuric acid in 20% yield.[70] Unfortunately, the observed yield of the reaction did not exceed 1% despite several attempts. Hence another method, described by Ranu and Jana,[71] was used. They claim to reach up to 92% yield of the sulfide after heating equimolar amounts of thiophenol and *t*-butanol for 1.5 h at 60 °C in an ionic liquid, 1-pentyl-3-methylimidazolium bromide. The ionic liquid was prepared according to literature by ultrasound irradiation of 1-methylimidazole and 1-brombutane.[72] The reaction with thiophenol and *t*-butanol was heated for 3 days, instead of 90 min, to 60 °C. Although the reaction was monitored by thin layer chromatography (TLC) at least every twelve hours it was not possible to observe any progress and no product was obtained after workup.

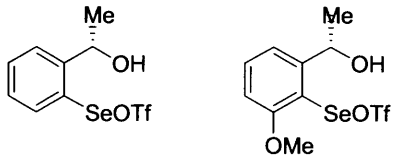
L. Breau and co-workers described another method for the synthesis of *t*-butyl(phenyl)sulfide **69** using acetic acid, acetic acid anhydride and perchloric acid (Scheme 2.31).[73]



Scheme 2.31: *Synthesis of racemic diselenide* ***54***

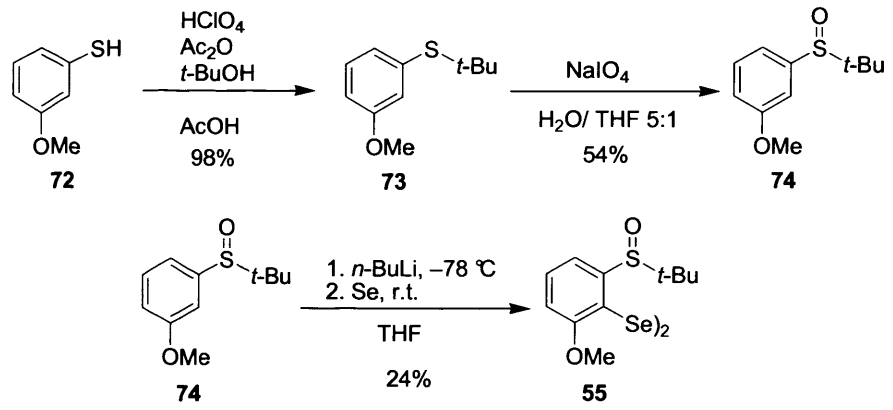
Employing this reagent mixture, the product was obtained in 97% yield and no further purification was necessary. Sulfide **69** was then oxidised to the sulfoxide with sodium periodate in 51% yield. Despite some changes in reaction conditions (temperature and reaction time) it was not possible to obtain sulfoxide **70** in better yields as the corresponding sulfone was formed in up to 45% yield as well. Additionally, some of the starting material was recovered after column chromatography. 2-(*t*-Butylsulfinyl)phenyl diselenide **54** was then synthesised by *ortho*-lithiation of sulfoxide **70** in THF in 39% yield as yellow foam. Although sulfoxides are in general very easy to crystallise, all attempts to do so failed in this case.

As the synthesis of diselenide **54** had proven to be successful, it seemed to be worthwhile to approach the synthesis of the analogue diselenide **55**, bearing an additional methoxy substituent in *ortho*-position to the diselenide (Scheme 2.33). Previous studies by Wirth and co-workers had shown that the methoxy group in 6-position on the aromatic system improved the enantiomeric excess of the chiral selenenylating reagent **71** (**16**: 91.5/ 8.5 d.r., **71**: 98/2 d.r.) (Scheme 2.32).[74]



Scheme 2.32: *Chiral selenenylating reagents by Wirth and coworkers*

Anticipating that this improvement could be observed with diselenides **54** and **55** as precursors for the selenenylation reactions as well, the synthesis of diselenide **55** with a methoxy group in 6-position was realised (Scheme 2.33).



Scheme 2.33: *Synthesis of racemic diselenide 55*

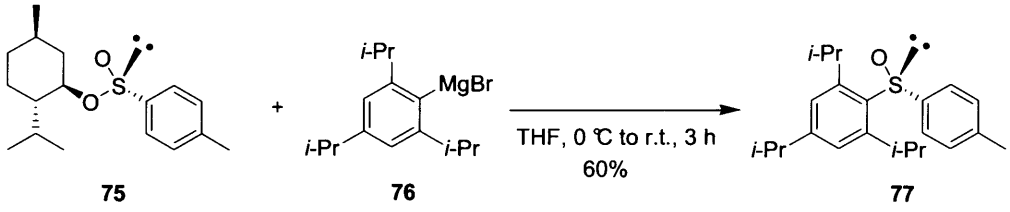
3-Methoxythiophenol **72** was used as starting material, following the same route that was used for the synthesis of diselenide **54**. Sulfide **73** was obtained in 98% yield and was used without further

purification for the following oxidation step. As was already observed in the previous synthesis, the formation of the sulfone could not be suppressed. Beside reisolated starting material and 54% of the sulfoxide, 35% of the corresponding sulfone were obtained. *Ortho*-lithiation of **74** and addition of elemental selenium then led to the formation of diselenide **55** in 24% yield.

2.2.4 Synthesis of Chiral Non-Racemic Diselenides with Sulfoxides as Centre of Chirality

The separation of the racemic diselenides **50**, **54** and **55** by HPLC using a chiral column is, if at all possible, very time-consuming. The general possibilities of separation by co-crystallisation or enzymatic resolution did not seem to be very promising and rather elaborate. Therefore, it was considered more straightforward to synthesise the sulfoxides in a stereoselective manner.

The successful synthesis of diselenide **50** was encouraging at first and the separation of the two enantiomers seemed to be possible with a HPLC method. A major drawback in this approach was the retention time of more than 80 minutes for the first isomer on a preparative *Chiracel® OD* column. As there was no easy route to synthesise diselenide **50** enantioselectively, it was decided to attempt the synthesis of a similar chiral sulfoxide (**77**) using the commercially available (–)-(1*R*,2*S*,5*R*)-menthyl-(*S*)-4-toluenesulfinate **75** (Scheme 2.34). The substitution of the menthyl group can be performed with any Grignard reagent, but it has to be taken into account that in the next step a lithium base is required for the *ortho*-lithiation which prevents the use of any structures with highly acidic protons. An ideal choice seemed to be (2,4,6-triisopropyl)phenylmagnesium bromide **76** which can not be *ortho*-lithiated at the 2-position and which only provides slightly acidic protons.

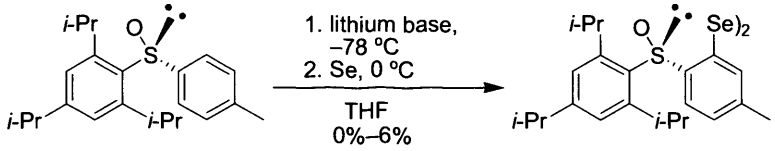


75 **76** **77**

Scheme 2.34: *Synthesis of sulfoxide 77*

The Grignard reagent **76** was prepared according to a standard procedure from (2,4,6-triisopropyl)phenyl bromide and magnesium in THF.[63] The reagent solution was directly added to sulfinate **75** in THF at 0 °C to afford (*R*)-1-(2,4,6-triisopropylphenyl sulfinyl)-4-methylbenzene **77** in 60% yield. The following *ortho*-lithiation was very challenging. Reaction with *n*-butyllithium in THF at –78 °C led to a nucleophilic attack on the sulfur atom and therefore a mixture of products of which 1,3,5-triisopropylbenzene, *n*-butyl-(4-methylphenyl)sulfoxide and dibutyl diselenide could be isolated.

Therefore a non-nucleophilic lithium base, lithium diisopropylamine, was used. Under the same conditions as described above, most of the starting material along with 6% of the product and some unidentified side products were obtained (Scheme 2.35). Increasing the temperature to 0 °C after addition for 2 h or stirring at room temperature did not increase the yield.

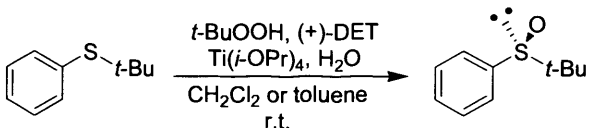


77 **78**

Scheme 2.35: *Synthesis of diselenide 78*

To improve the yield of diselenide **78**, another base, lithium 2,2,4,4-tetramethylpiperidine (LiTMP), was tested. In THF at –78 °C this reaction afforded product in 4% yield along with starting material. No side products were obtained. In a further attempt the reaction mixture was stirred at 0 °C for four hours and checked every hour by quenching with deuterated water. According to the NMR spectra of these reactions, no *ortho*-lithiation took place and no side products had formed. Then the solution was warmed to room temperature and stirred for another five hours. The mixture was tested for progress in the same manner every 30 minutes. Although no reaction could be detected, the mixture was quenched with selenium. Only traces of the product were found in the NMR spectrum, which was in agreement with the previous D_2O quenched samples. The reaction was repeated at 40 °C for one hour, but this led to a complex reaction mixture. Further attempts to improve the outcome of this reaction were deferred and the chiral non-racemic syntheses of diselenides **54** and **55** were pursued instead.

As already mentioned in the introduction of Chapter 2.2.2, there are several possible methods to obtain chiral non-racemic sulfoxides. Kagan *et al.* established an efficient asymmetric oxidation of sulfides to sulfoxides with a modified Sharpless reagent for asymmetric epoxidation.[43] Ti(O*i*-Pr)$_4$, diethyltartrate, H_2O and *t*-butylhydroperoxide in dichloromethane are used to oxidise sulfides to enantiomerically enriched sulfoxides.



69 (*S*)-**70**

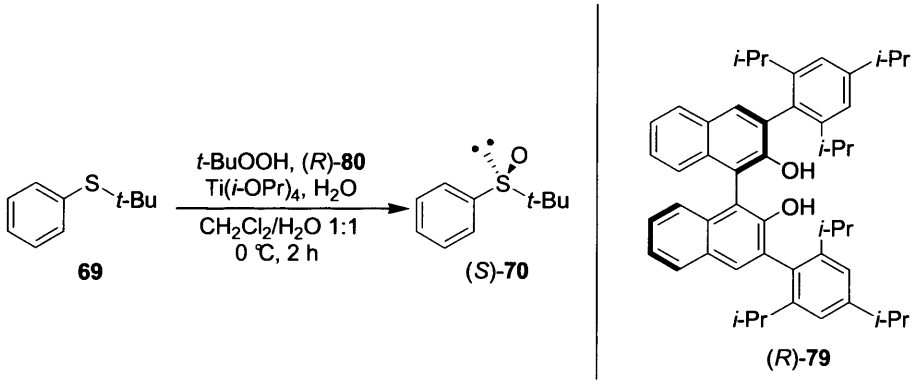
Scheme 2.36: *Attempted enantioselective synthesis of sulfoxide (S)-70*

Although there is no reference to *t*-butyl(phenyl)sulfide **69** as starting material, the reaction was tested with sulfoxide (*S*)-**70** (Scheme 2.36). Following this procedure, using dichloromethane as solvent, *t*-butyl(phenyl)sulfoxide **70** was obtained in 30% yield, along with starting material and sulfone.

Unfortunately, HPLC analysis showed no enantiomeric excess. The reaction was repeated in toluene, which resulted in 22% yield of the sulfoxide, again along with starting material and the corresponding sulfone. The enantiomeric excess of this reaction according to HPLC analysis was 2%.

Another communication by Jia and co-workers used a similar reagent combination with (*S*)-BINOL instead of diethyltartrate and toluene for solubility reasons.[75] They claimed better yields and enantiomeric excesses with comparable sulfides, however *t*-butyl(phenyl)sulfide was again not used as starting material. Nevertheless, the reaction was carried out according to their procedure and afforded 25% of the sulfoxide **70** along with starting material and sulfone (1:1) after 43 h. The enantiomeric excess (10%) had slightly improved compared to the previous attempt. The reaction was repeated with a shorter reaction time (19 h) to suppress the formation of the sulfone, but the ratios of starting material, sulfoxide and sulfone were still about 1:1:1.

In a last attempt to synthesise chiral non-racemic (*S*)-**70** via an oxidative process, **69** was treated with the established reagent combination $Ti(Oi\text{-}Pr)_4$, H_2O and *t*-butylhydroperoxide together with (*R*)-**79** [(*R*)-3,3'-bis(2,4,6-triisopropylphenyl)-2,2'-dihydroxy-1,1'dinaphthyl] as chiral ligand to the titanium (Scheme 2.37). However, the obtained sulfoxide was only isolated as racemic mixture.

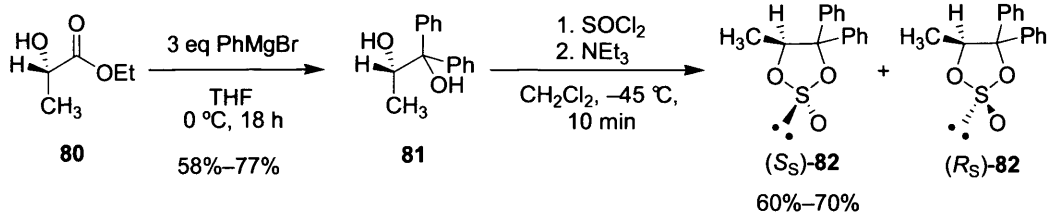


Scheme 2.37: *Attempted non-racemic synthesis of sulfoxide (S)-**70** with ligand (R)-**79***

As the chiral oxidative methods had failed, the attention was turned towards the nucleophilic substitution on chiral, diastereomerically pure cyclic sulfites, following a synthesis route developed by Kagan and co-workers. This method, which was already outlined in Chapter 2.2.2, was used to prepare the chiral non-racemic sulfoxide (*S*)-**70** from a cyclic chiral sulfite **82**, which can be synthesized in two steps from (*S*)-ethyl lactate **80** (Scheme 2.38).

Lactate **80** was reacted with 3 equivalents of phenylmagnesium bromide in THF at 0 °C to give (*S*)-diol **81** as a colourless oil in up to 77% yield after column chromatography. Compound **81** was dissolved in dichloromethane and a solution of thionyl chloride in dichloromethane was added at –40 °C. Then triethylamine in dichloromethane was added dropwise at this temperature. This unusual way of addition was established by Kagan and co-workers, who attained a selectivity of 9:1 in favour

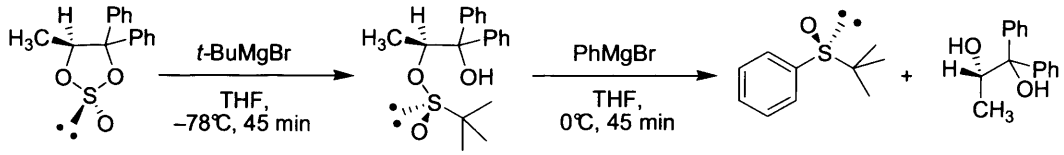
of the *trans*-sulfite (S_S)-**82** [(2*R*,5*S*)-*trans*-4,4-diphenyl-5-methyl-1,3,2-dioxathiolane-2-oxide]. After the cyclisation reaction, (S_S)-**82** was obtained in 60% to 70% yield, in all cases however only with a 3.5 fold excess over the *cis*-sulfite (R_S)-**82**. The reason for the low selectivity compared to the literature could not be identified.



80 **81** (S_S)-**82** (R_S)-**82**

Scheme 2.38: *Synthesis of cyclic chiral sulfites (S_S)-82 and (R_S)-82*

Kagan *et al.* stated that, in the first ring-opening step, Grignard reagents are more successful because in comparison to their organolithium equivalents they are less reactive and do not lead easily to the symmetric sulfoxides. Therefore, instead of *t*-buyllithium, *t*-butylmagnesium bromide was used, either as a commercially available 2 molar solution in diethyl ether or synthesized from *t*-butyl bromide with elemental magnesium in THF under reflux (Scheme 2.39). However, *t*-butylmagnesium bromide crystallises at room temperature in THF and can only be partially redissolved by warming the mixture over 35 °C. This gave rise to the problem that the determination of the concentration of the Grignard reagent was difficult. However, the concentration of the Gignard reagent in this reaction is crucial to avoid an over-reaction and, furthermore, the addition of *t*-butylmagnesium bromide needs to occur at –78 °C. It is to assume that due to these reasons the yields obtained were quite low (just up to 16%). Some of these problems could be avoided by a change of solvent to diethyl ether instead of THF, which could be demonstrated by the employment of a commercially available 2 molar solution of *t*-butylmagnesium chloride. These reactions led to moderate yields of (*S*)-**70** in 46%.

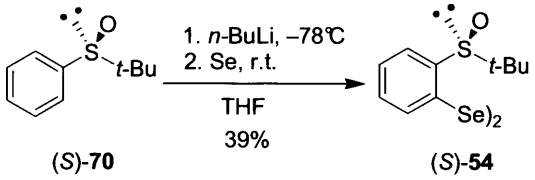


(S_S)-**82** **83** (*S*)-**70** **81**

Scheme 2.39: *Synthesis of chiral non-racemic t-butyl(phenyl)sulfoxide (S)-70*

In the next step, **83** was treated with phenylmagnesium bromide in THF at room temperature, which afforded the desired sulfoxide (*S*)-**70** in 46% yield and diol **81** in 40% yield which could be reused after purification. The optical rotation measured obtained with (*S*)-**70** in dichloromethane was $[\alpha]_D^{20} = -188$, which is in accordance with published results ($[\alpha]_D^{20} = -175$).[58b]

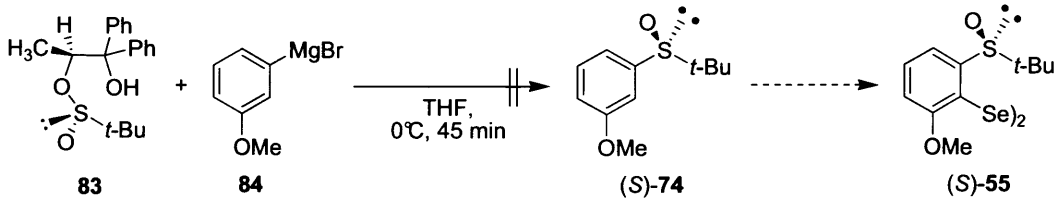
(*S*)-*t*-Butyl(phenyl)sulfoxide was then *ortho*-lithiated with *n*-butyllithium in THF and treated with selenium to afford the diselenide (*S*)-**54** in 39% yield.



Scheme 2.40: *Synthesis of chiral non-racemic diselenide (S)-54*

(*S*)-Bis-[2-(*t*-butylsulfinyl)phenyl] diselenide (*S*)-**54** is a yellow crystalline substance with an optical rotation of $[\alpha]_D^{20} = -65.5$. In contrast to the racemic mixture of the diselenide *rac*-**54** it was possible to obtain a crystal structure of diselenide (*S*)-**54** (Chapter 2.2.5) after recrystallisation from pure diethyl ether.

It was also attempted to synthesise (*S*)-bis-[2-(*t*-butylsulfinyl)-6-methoxyphenyl] diselenide (*S*)-**55** via the same route as described above. Therefore, 3-methoxyphenyl magnesium bromide **84** was synthesised from 3-anisyl bromide and reacted with **83** (Scheme 2.41). However, this reaction resulted in a complex mixture of products from which neither the starting material nor the expected product **87** could be isolated. The methoxy group in 3-position seems to enhance the reactivity of the Grignard reagent significantly, which leads to a range of side reactions.

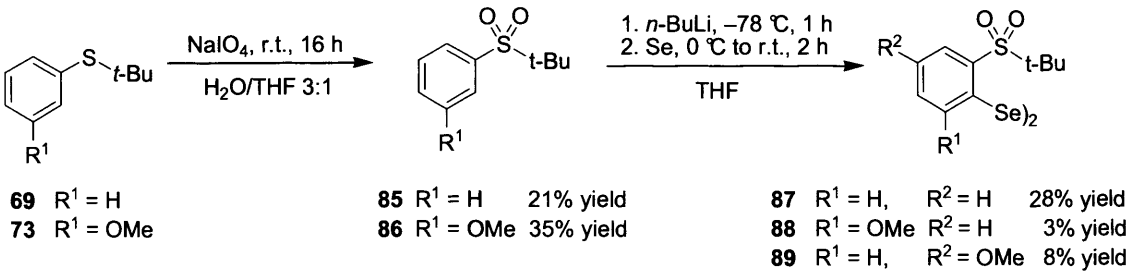


Scheme 2.41: *Attempted synthesis of chiral non-racemic sulfoxide (S)-55*

2.2.5 Synthesis of Diselenides with Sulfones as Auxiliaries

The synthesis of the previously described racemic sulfoxide-containing diselenides included the oxidation of sulfide **69** to the sulfoxide (Chapter 2.2.2). The low yield of the obtained sulfoxide during this reaction is due to the partial over-oxidation to sulfone **85**, which was obtained in 21% yield. A very similar reactivity was observed during the oxidation of *t*-butyl[(3-methoxy)phenyl] sulfide **73**, which resulted as well in the formation of *t*-butyl[(3-methoxy)phenyl]sulfone **86** in 35% yield, together with the sulfoxide (54%). The availability of the sulfones led to the idea to synthesise the corresponding diselenides as shown in Scheme 2.42 for structure related studies.

2-*t*-Butyl(phenylsulfonyl) diselenide **87** was prepared from 2-*t*-butyl(phenyl)sulfone **85** via *ortho*-lithiation in THF and addition of elemental selenium in 28% yield. A crystal structure was obtained after recrystallisation from dichloromethane (Chapter 2.2.5). Using sulfone **86** as starting material in the reaction under the above mentioned conditions (*n*-BuLi, THF, –78 °C; Se, r.t.) led to a complex reaction mixture. However, it was possible to identify two products out of this mixture after column chromatography. The two diselenides **88** and **89** were clearly identified after recrystallisation from dichloromethane by X-ray structure analysis (Chapter 2.2.5) and obtained in 3% and 8% yield, respectively.



69 R^1 = H
73 R^1 = OMe

85 R^1 = H 21% yield
86 R^1 = OMe 35% yield

87 R^1 = H, R^2 = H 28% yield
88 R^1 = OMe R^2 = H 3% yield
89 R^1 = H, R^2 = OMe 8% yield

Scheme 2.42: *Synthesis of diselenides with sulfones as auxiliaries*

2.2.6 Comparison of Crystal Structures

Beside NMR analysis and mass spectrometry, X-ray crystallography of a single crystal is a valuable tool for the structure determination of a new compound. This method allows the determination of the arrangement of atoms within a crystal by visualising the electron density within this crystal. The electron density pattern can be obtained when a crystal is struck with a beam of X-rays. The beam gets scattered and this leads to a specific diffraction pattern of regularly spaced spots (reflections). The positions of the atoms in the crystal can be determined as well as their chemical bonds using two-dimensional images. These images are taken at different rotations and can be converted into a three-dimensional model of the density of electrons within the crystal, using Fourier transformations and known chemical data of the sample.

The chiral non-racemic sulfoxide-containing diselenide (*S*)-**54** and the sulfone-containing diselenides **87**, **88** and **89** are crystalline yellow compounds which produced single crystals after recrystallisation (Figure 2.1). These four diselenides were subjected to single-crystal X-ray diffraction and are compared with each other and diselenide **71** which was synthesised by Wirth and co-workers. According to their studies, the selenenylating reagent obtained from diselenide **71** showed a very good degree of stereoinduction (up to 98:2 d.r.).

As shown in Table 2.2, the direct comparison between diselenide (*S*)-**54** and **71** reveals that the oxygen attached to the chiral centre has *no* interaction with the selenium atoms in the solid state. The

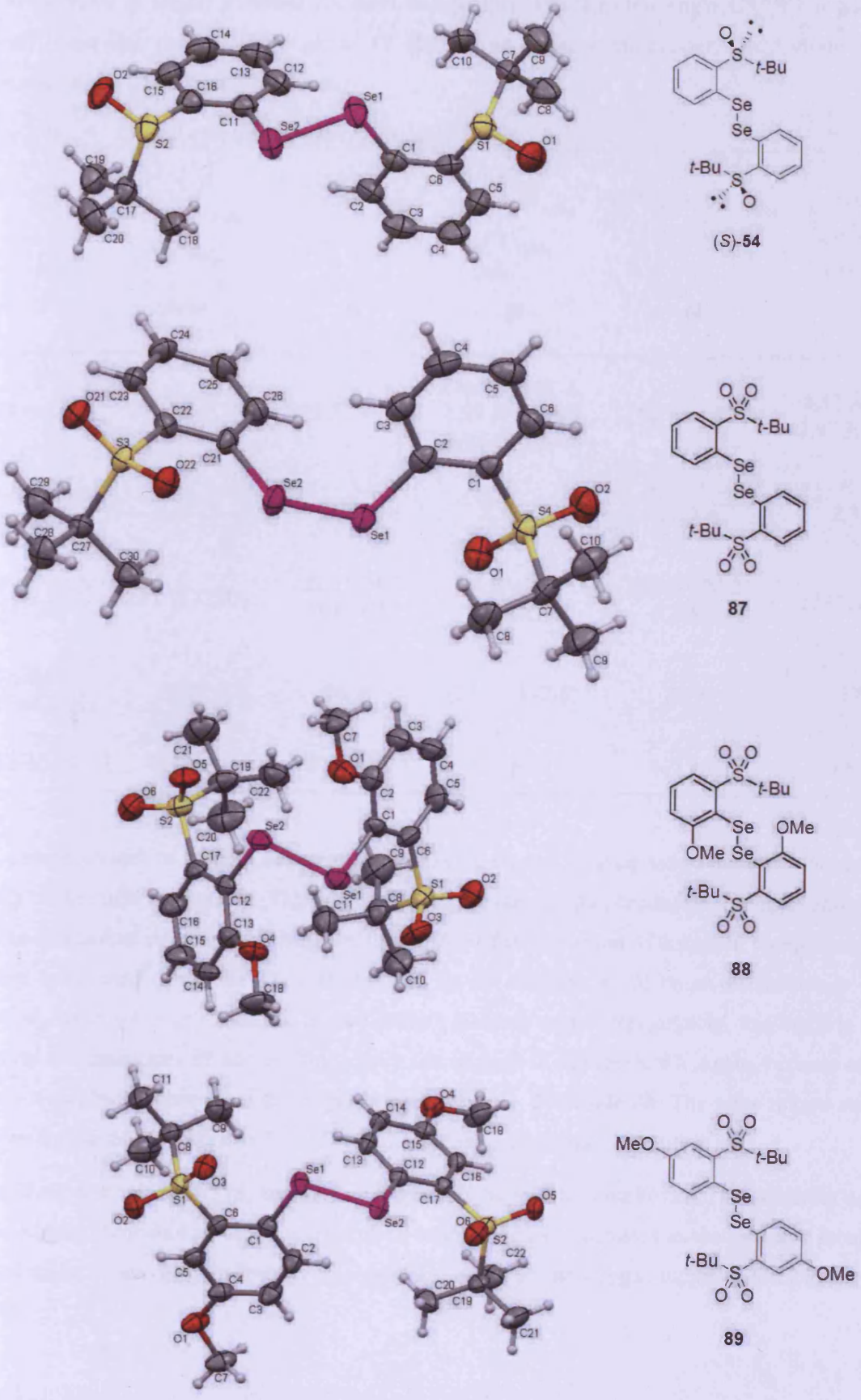
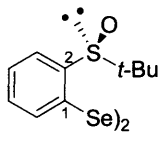
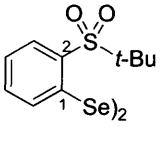
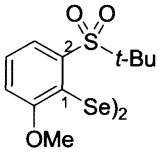
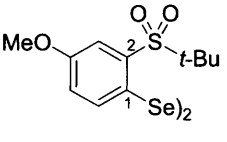
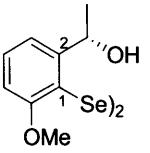


Figure 2.1: *Crystal structures of diselenides (S)-**54**, **87**, **88** and **89***

Se–Se distance is almost identical for both compounds. The dihedral angle C^1C^2SO in (*S*)-**54** is slightly larger than the C^1C^2CO angle of **71** which is an effect of the bulkier *t*-butyl group. For the same reason, the CSeSeC angle is larger.

Table 2.2: *Crystal structure comparison between diselenides*

	 (*S*)-**54**	 **87**	 **88**	 **89**	 **71**
Se–O distance	4.65 Å	2.79 Å, 4.73 Å	2.96 Å, 4.81 Å, 2.99 Å (OMe), 2.97 Å (OMe)	2.78 Å, 4.72 Å	4.42 Å (OH), 2.97 Å (OMe)
Se–Se bond distance	2.31 Å	2.32 Å	2.35 Å	2.23 Å	2.33 Å
dihedral angle C^1C^2XO	147° (CCSO)	152.5°, 24.7° (CCSO)	156.2°, 27.8° (CCSO)	148.8°, 20.2° (CCSO)	131° (CCCO)
CSeSeC dihedral angle	89.5°	96.2°	113.7°, 112.5°	78.9°	77.5°
^{77}Se-NMR	436 ppm	476 ppm	465 ppm	467 ppm	366 ppm

The downfield shift of 70 ppm observed in the ^{77}Se NMR can be assigned to the different electronic effects of the sulfur substituent. This can be backed up, taking into account the chemical shifts of the sulfone-substituted diselenides, which are shifted downfield by about 100 ppm in comparison to the alcohol substituted diselenide **71**. Although the Se–Se distance in all these diselenides is almost identical, there is a huge difference in the CSeSeC dihedral angles. Remarkably, this angle is almost identical for diselenides **89** and **71**, but slightly forced open in diselenide **87**. Again, because of steric effects it can be presumed that this angle is even wider in diselenide **88**. The same reason seems to account for the dihedral angles of C^1C^2SO in the sulfone-containing diselenides.

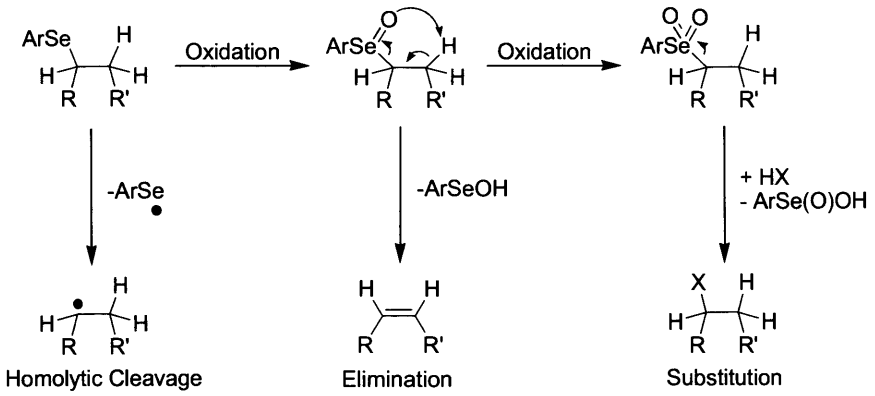
In the three diselenides, **87**, **88**, and **89**, one oxygen of the sulfone moieties is in coordinating distance to the adjacent selenium atom and in case of **88** even at the same distance as the methoxy group. The second sulfoxide-oxygen however, is in a similar distance as the oxygen atoms in diselenides (*S*)-**54** and **71**.

3. New Selenium Electrophiles and Their Reactivity

3.1 Generation and Reactivity of Selenium Electrophiles

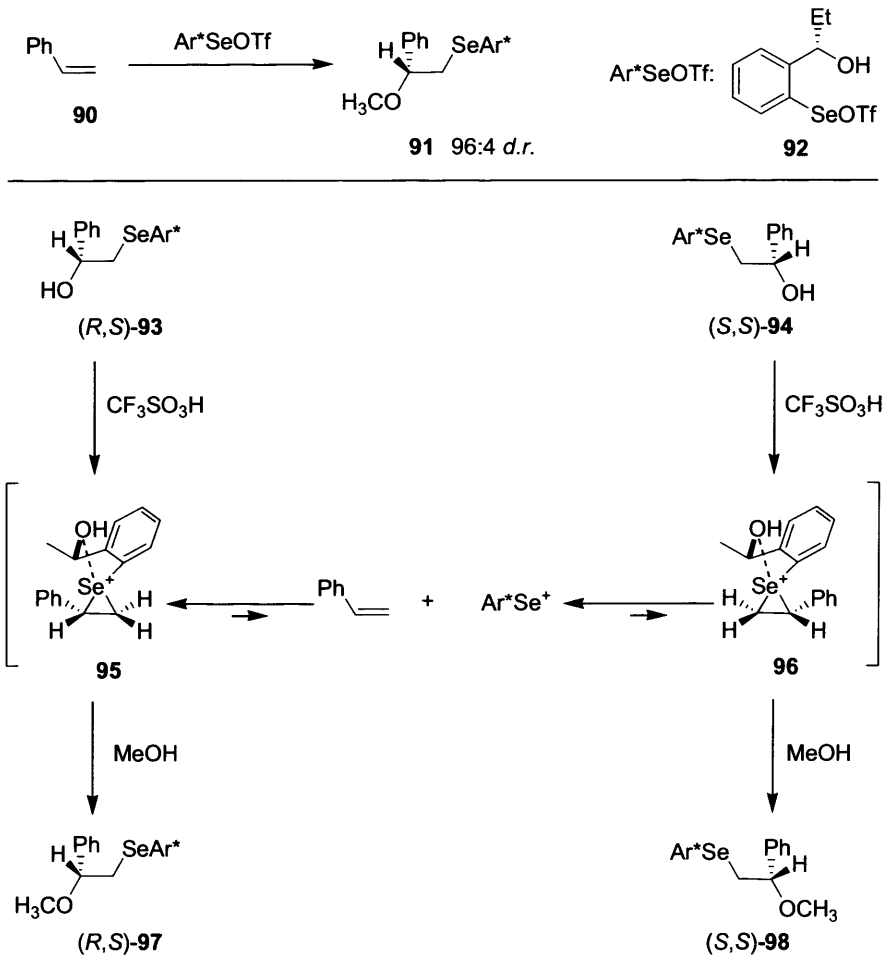
Phenylselenenyl chloride and phenylselenenyl bromide are commercially available and can be easily produced from diphenyl diselenide by treatment with sulfuryl chloride or chlorine in hexane and with bromine in tetrahydrofuran, respectively. Other selenium electrophiles can be easily prepared from the corresponding diselenides employing the same reagents. However, to avoid the incorporation of the halide anions during the selenenylation reaction and a possible decrease in stereoselectivity it is possible to exchange the halide ion *in situ*. Silver salts such as triflate,[76] tetrafluoroborate,[77] hexafluorophosphate,[78] hexafluoroantimonate,[75] or tolylsulfonate[79] can be employed for this purpose. The selenium electrophiles can also be generated by oxidation with ammonium peroxodisulfate.[80a] Phenylselenyl sulfate is a very efficient reagent and can be generated via this route. Other reagents like KNO_3, [81] $Ce(NH_4)_2(NO_2)_6$, [82] $Mn(OAc)_3$, [83] [bis(trifluoroacetoxy)iodo] benzene [84] and diacetoxy iodobenzene[85] were also successfully employed to generate selenium electrophiles by oxidation from the corresponding diselenides. A third possibility is the generation of the phenylselenenyl cation via photosensitised single electron transfer from the diselenide to 1,4-dicyanonaphthalene.[86] However, the synthesis of selenium electrophiles is strongly depending on the reaction requirements. Very efficient and broadly applicable are triflate and sulfate counterions, which generally produce clean reactions. The preparation of the sulfate is easier than the generation of the triflate, but is has the drawback that it can not be employed with other functional groups which are easily oxidized.

The most important use of electrophilic phenylselenenyl reagents is the functionalisation of carbon-carbon double and triple bonds. The incorporated selenium moiety has relatively few direct applications, but the great synthetic importance is that it can be used for further useful transformations as shown in Scheme 3.1. The phenylseleno group can be substituted in several ways. Treatment with tin hydrides leads to homolytic cleavage of the carbon-selenium bond, and the generated carbon radicals can be used for subsequent radical reactions. The oxidation of the phenylseleno moiety to selenoxides leads to elimination products via the well known selenoxide elimination mechanism.



Scheme 3.1 *Deselenenylation strategies*

Further oxidation to the selenone results in the generation of a good leaving group, which can be substituted by a variety of nucleophiles. Likewise, the treatment with another equivalent PhSeX generates a selenonium ion which can be substituted by a nucleophile as well.



Scheme 3.2: *Mechanistic investigation of the asymmetric methoxyselenenylation of styrene*

The addition of optically active selenenylating reagents to carbon-carbon double bonds affords a mixture of two diastereomers. In some cases, these diastereomers can be separated and the subsequent deselenenylation leads to enantiomerically pure products. Asymmetric oxyselenenylation reactions with an external nucleophile (e.g. methanol) are often employed to test the efficiency of a new chiral selenium electrophile. The stereospecific *anti*-addition of an organoseleno-group and of an oxygen nucleophile is used for the preparation of simple as well as complex molecules.

Wirth and co-workers investigated the methoxyselenenylation of styrene in detail to establish the stereochemical course of the reaction (Scheme 3.2).[87]

The reaction of styrene with (*S*)-selenenyltriflate **92** leads to the selective formation of addition product **91** with a diastereomeric ratio of 96:4. The newly formed stereocentre has (*R*)-configuration which corresponds to a favored *re*-attack of the styrene double bond. The determining step for the stereochemistry is the formation of seleniranium intermediates during the attack of the alkene onto the selenium electrophile.[1,88] This suggests the preferential formation of one seleniranium intermediate, which is a reversible process as shown with competitive experiments. Hence, these results indicate a difference in stability for the respective three-membered ring systems. Wirth and co-workers independently synthesised chiral β-hydroxyselenides with the configuration of (*R,S*)-**93** and (*S,S*)-**94**. Protonation of these compounds and an intramolecular S_N2 displacement by the selenium reagents generated the seleniranium intermediates **95** and **96**. Intermediate **95** reacted with methanol without loss of stereochemical information to the expected product **97** with (*R,S*)-configuration. Corresponding to a *si*-attack of **92** onto styrene, intermediate **96** was assumed to be less stable and after reaction with methanol indeed a mixture of (*S,S*)-**98** and (*R,S*)-**97** was obtained. This indicated the conversion of **96** into **95** via a decomplexation–complexation mechanism (Scheme 3.2).

An approximated energy diagram, shown in Figure 3.1, highlights the differences in ΔG during the formation of intermediates **95/96** and (*R,S*)-**97**/(*S,S*)-**98** starting from styrene and **92**. According to calculations by Wirth *et al.* **95** is about 2.8 kcal/mol more stable than **96**. This suggests a kinetically controlled reaction, where both intermediates (**95/96**) are less stable than either [styrene+Ar*Se^+] or (*R,S*)-**97**/(*S,S*)-**98**. The reaction of **95** or **96** with a nucleophile (methanol) however is thermodynamically controlled and should lead to products of equal energy via equal ΔG values. These ΔG values however must be smaller than the ΔG values for the conversion of **95** or **96** to [styrene+Ar*Se^+], as the preferred products in these reactions are (*R,S*)-**97**/(*S,S*)-**98**. The reactions of (*R,S*)-**93** and (*S,S*)-**94** (not included in Figure 3.1) to the intermediates **95** and **96** are thermodynamically controlled.

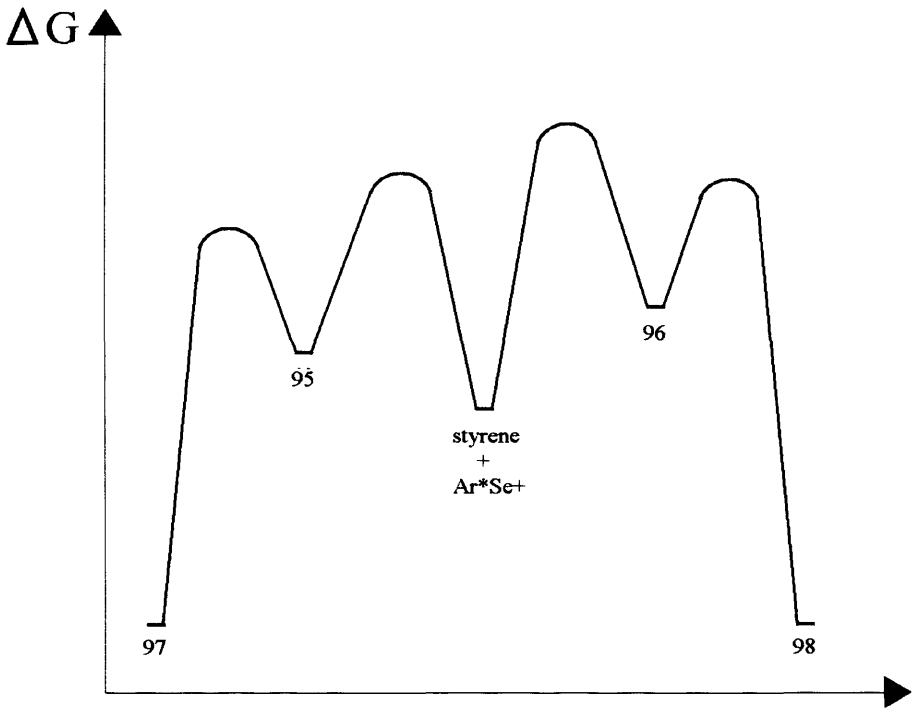
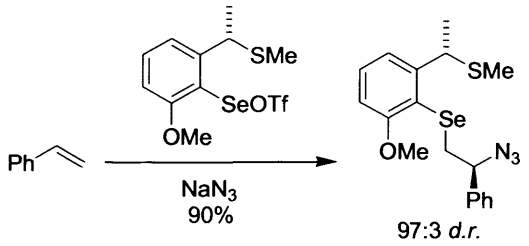


Figure 3.1: *Energydiagram for the asymmetric methoxyselenenylation of styrene shown in Scheme 3.2*

Recent advances with selenenylation reactions include an asymmetric azido selenenylation reaction by Tiecco *et al.* (Scheme 3.3) which allows further transformations into aziridines and triazoles.[89] It is remarkable that his reaction occurs with a very high level of facial selectivity and with "Markovnikov" orientation.

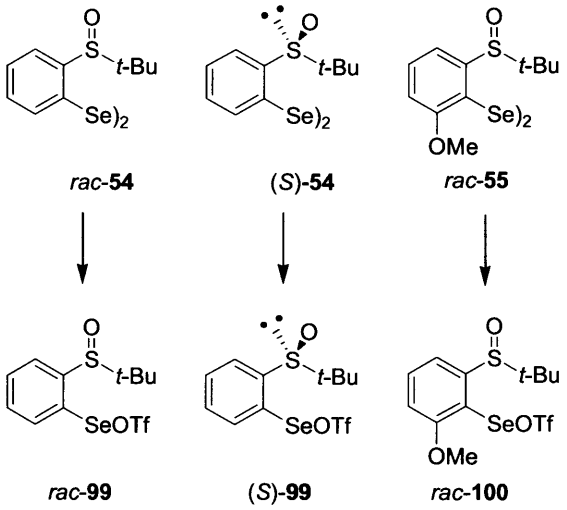


Scheme 3.3: *Asymmetric azido selenenylation reaction by Tiecco et al.*

3.2 Reactivity of Sulfoxide-Containing Selenium Electrophiles

Bis-[2-(*t*-Butylsulfinyl)phenyl] diselenide [*rac*-**54**], (*S*)-bis-[2-(*t*-butylsulfinyl)phenyl diselenide [(*S*)-**54**] and bis-[2-(*t*-butylsulfinyl)-6-methoxyphenyl] diselenide [*rac*-**55**] (syntheses see Chapters 2.2.3 and 2.2.4) were used for the following methoxyselenenylation reactions to establish their ability to influence the stereochemical outcome of these reactions. As already stated in the introduction, there is a broad choice of methods and reagents available to generate the selenium electrophiles from the

corresponding diselenides. With respect to the nature of the chiral centre of the diselenides, a sulfoxide moiety, the generation with halides was preferred over the oxidative methods. Because of the good results which according to literature were obtained with triflates as counterions, silver triflate was used for the halogen exchange reaction (Scheme 3.4).

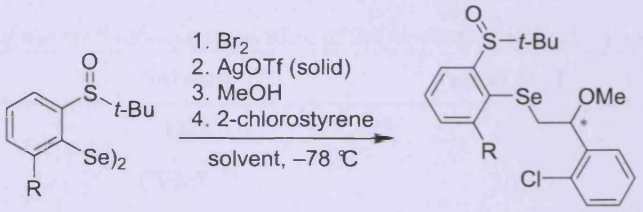


Scheme 3.4: *Used diselenides and their corresponding selenenyl triflates*

Hence, a typical procedure proceeded via the generation of the selenenyl bromide, the exchange of the bromine counteranion with the less nucleophilic triflate, the addition of the selenenyl cation onto the carbon-carbon double bond and the attack of a nucleophile which led to the product formation. For this one-pot procedure, 0.1 mmol of the diselenide was dissolved in 4 ml of solvent, cooled to −78 °C, and 100 µl of a 1M solution of bromine in carbon tetrachloride were added to generate the selenenyl bromide. Upon addition of silver triflate and stirring for 25 minutes, the silver bromide precipitated from the solution. Typically, then styrene was added followed by the addition of methanol after stirring the mixture for 5 minutes at −78 °C. The reaction was further stirred for 2 hours at the same temperature. The diastereomeric ratio (*d.r.*) of the products obtained with racemic selenenyl triflate *rac*-**99** was determined by NMR, which is a reasonable approach, taking Wirth's observations into account.[85]

Initially *rac*-**99** and *rac*-**100** were screened with 2-chlorostyrene as substrate in different solvents (Table 3.1). The best selectivities with triflate *rac*-**99** were found using dichloromethane (11:1) or chloroform (7:1). These solvents also proved to give the best yields (up to 48%). When the reactions were carried out in polar ethers like tetrahydrofuran and cyclopentyl methyl ether (CPME) the selectivities dropped significantly to 4:1. However, in diethyl ether the selectivity was slightly better (5:1), which could be caused by the difference in the solvation of the diselenide. The diastereomeric ratio in a 4:1 mixture of diethyl ether and dichloromethane was again observed as 5:1, presumably because of the high excess of the more polar solvent. The reaction was not carried out in more unpolar

solvents like hexane or toluene, as the diselenide is insoluble in these solvents. It is assumed that the obtained selectivities are a synergetic effect of the coordination of the oxygen from sulfoxide to the selenium and the bulky *t*-butyl group. The coordination of the oxygen would be stronger in less polar solvents and would therefore force the chiral centre nearer to the reaction centre.



R = H *rac*-**54**
R = OMe *rac*-**55**

R = H **101**
R = OMe **102**

Scheme 3.5: *Methoxyselenenylation of 2-chlorostyrene with methanol in different solvents*

Table 3.1: *Selectivities of the methoxyselenenylation of 2-chlorostyrene* with rac-**99** *in several solvents*

Entry	Solvent	Yield [%]	*d.r.*[a]
1	THF	29	4:1
2	CPME[b]	29	4:1
3	Et_2O	36	5:1
4	Et_2O/CH_2Cl_2 4:1	41	5:1
5	CH_2Cl_2	41	11:1
6	$CHCl_3$[c]	48	7:1

[a] Determined from NMR spectra of crude products. [b] CPME: cyclopentyl methyl ether. [c] Reaction was performed at –50 °C.

Interestingly, the colour of the selenium electrophile with the triflate anion is dependent on the solvent (Figure 3.2) and can be used as an indicator for the progress of the reaction. This is not the case with *rac*-**100** which always results in yellow mixtures.

Figure 3.2: *Colour of corresponding selenenyl bromides (orange in all solvents) and selenenyl triflates* ***99*** *in different solvents (THF: purple, CPME: red, CH_2Cl_2: green)*

Surprisingly, triflate *rac*-**100** was less reactive and much less selective under the same reaction conditions (Table 3.2). The highest diastereomeric ratio using 2-chlorostyrene giving product **102** was observed in tetrahydrofuran (3:1), but with low yield (18%). In chloroform the yield was better, as

The reactivity of selenenyltriflates *rac*-**99**, (*S*)-**99** and *rac*-**100** towards different substrates was then investigated employing methanol as standard nucleophile.

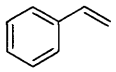
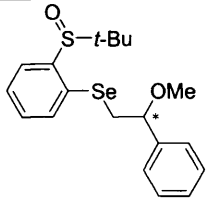
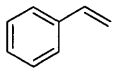
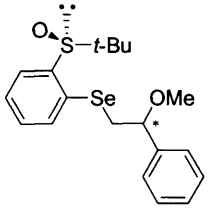
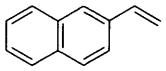
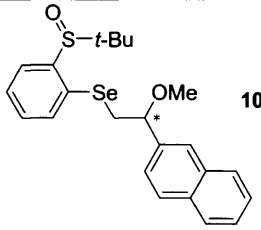
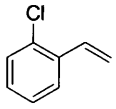
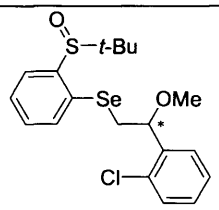
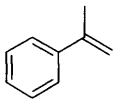
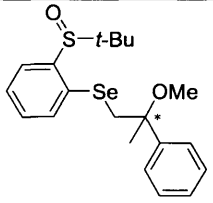
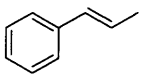
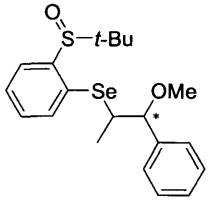
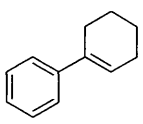
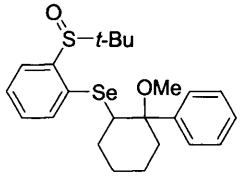
The monosubstituted double bonds of styrene and 2-vinylnaphthalene (Table 3.3, entries 1, 2 and 3) showed reasonable selectivities with diastereomeric ratios of 5:1, although they were performed in THF. Additionally, the yields obtained for **103** and **103a** were reasonable compared with the other reactions.

A chlorine substituent in the 2-position of the aromatic system (entry 4) enhanced the selectivity considerably (11:1) and led to **101** in 41% yield. Generally, the use of sterically more hindered alkenes led to lower yields (entries 5–7) between 30% and 38%. However, β-substitution on the styrene enhanced the selectivity (entries 6 and 7) to 11:1 and 9:1, respectively. The slightly electron deficient double bonds of methyl cinnamate and 3-nitrostyrene were not reactive enough under the conditions of the methoxyselenenylation reaction.

The diastereomeric ratios obtained using the enantiomerically enriched (*S*)-**99** and the racemic selenenyltriflate *rac*-**99** are identical (5:1). This observation is in agreement with Wirth's findings mentioned in the introduction (Chapter 3.1). During the attack of an alkene onto a chiral selenium electrophile, the formation of one of the two possible seleniranium intermediates is preferred. Assuming for example that a selenium electrophile with (*S*)-configuration would lead to a preferential formation of a new (*R*)-configured stereocentre, then the same would be true for the opposite (*R*)-configured selenium electrophile. This would lead to the formation of a new (*S*)-stereocentre, and in both cases the less favoured enantiomeric pairs of (*S*,*S*)- and (*R*,*R*)-configurations are suppressed. As could be shown with the results obtained of products **103** and **103a**, it is legitimate to use the racemic selenenyl triflate in the present experiments for the determination of the diastereomeric excess from the crude NMR spectra. Whereas the optical rotation obtained for **103** was $[\alpha]_D^{20} = 0$ as expected, the value for **103a** was $[\alpha]_D^{20} = -128$.

The relative stereochemistry of products **101** to **109** was not determined. A possible approach would be the homolytic cleavage of the carbon selenium bond of **103a** with $SnBu_3H$, which would remove the selenium moiety, but leaving the other chiral centre intact, leading to a mixture of enantiomers reflecting the selectivity observed during the methoxyselenenylation reaction. The enantiomerically pure synthesis of one of these enantiomers via a different route (e.g. stereoselective reduction of the keto-analogue and methylation of the alcohol) would allow the comparison of both of the products and hence the determination of the absolute stereochemistry of products **101** to **109**.

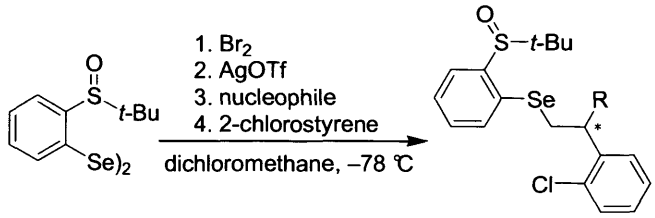
Table 3.3: *Reactivity of rac-**99** and (S)-**99** towards different styrenes*

Entry	Alkene	Solvent	Yield [%]	*d.r.*[a]	Product
1		THF	52	5:1	 **103**
2[b]		THF	50	5:1	 **103a**
3		THF	32	5:1	 **104**
4		CH_2Cl_2	41	11:1	 **101**
5		CH_2Cl_2	38	4:1	 **105**
6		CH_2Cl_2	30	11:1	 **106**
7		CH_2Cl_2	30	9:1	 **107**

[a] Determined from NMR spectra of crude products. [b] Reaction carried out with selenenyl triflate *(S)-**99***

As mentioned above, selenenyl triflate *rac*-**100** was used for a similar reactivity study with different styrenes. The solvent screening had already shown that *rac*-**100** was much less selective than *rac*-**99** using 2-chlorostyrene as substrate. As this observation could be due to the substrate used, two other styrenes were tested. The non-substituted styrene lead to a diastereomeric ratio of 2:1 with 24% yield for **108**, and α-methylstyrene led to a product ratio of 1:1 and 22% yield **109**. Further investigations using diselenide *rac*-**100** were deferred, due to these rather disappointing results.

In a last series of reactions, the influence of the nature of the nucleophile on the diastereoselectivity was investigated, employing triflate *rac*-**99** in the selenenylation reaction with 2-chlorostyrene as substrate (Scheme 3.7, Table 3.4).



rac-**54** **101, 110-114**

Scheme 3.7: *Selenenylation reaction of 2-chlorostyrene with different nucleophiles*

Table 3.4: *Reactivity of rac-99 towards 2-chlorostyrene and different nucleophiles*

Entry	Nucleophile	Product	Yield [%]	*d.r.*[a]
1	methanol	**107**	41	11:1
2	ethanol	**110**	47	8:1
3	*i*-propanol	**111**	47	8:1
4	*t*-butanol	**112**	30	6:1
5	benzyl alcohol	**113**	30	3.5:1
6	benzoic acid	-	traces	-
7	$TMSN_3$	**114**	35	6:1

[a] Determined from NMR spectra of crude products.

The reaction was tested with several oxygen, nitrogen and sulfur nucleophiles. Table 3.4 presents the results obtained with different oxygen nucleophiles. The yields realised with small nucleophiles like methanol, ethanol and *i*-propanol are comparable and better than that obtained with *t*-butanol, which can be assumed to occur due to the steric strain. The diastereomeric ratios are decreasing from methanol to ethanol and *i*-propanol to *t*-butanol.

The nucleophilicity of these alcohols can be influenced by several properties,[90] of which: (a) the solvation energy of the nucleophile; (b) the bond strength of the new Nu-C bond formed; (c) the electronegativity of the attacking atom; (d) the polarisability of the attacking atom; and (e) the steric bulk of the nucleophile are most important.

The first characteristic expresses that a strong solvation leads to an increase in the activation energy, as the solvation shell of the anionic nucleophile needs to be disrupted. The second suggests that if the newly formed bond is very stable, the transition state in a S_N2 reaction shows a higher stability as well. This leads overall to a decrease in the activation energy. The third point takes into account that a strongly electronegative nucleophilic centre is less reactive because the electrons, which are necessary for the bond formation, are more tightly bound to the nucleus. This observation is closely related to the fourth statement, the polarisability of the electron shell. Finally, a more sterically hindered nucleophile is less reactive than an unhindered centre, because it can not avoid the non-bonded repulsions in a transition state.

Taking these points into account, it can be assumed that the most important influence in the selenenylation reactions described above is the steric bulk which increases from methanol to ethanol and *i*-propanol to *t*-butanol. However, the selectivity obtained with benzyl alcohol (3.5:1) can not be explained by the steric bulk involved. In this case it should be expected that the diastereoselectivity would be better than 6:1 (as for *t*-butanol). In Chapter 3.1 it was already highlighted that experiments by Wirth and co-workers suggest the preferential formation of one seleniranium intermediate, which is a reversible process due to differences in stability. If the rate of the epimerisation of the three-membered ring systems is higher than that of the nucleophilic attack of the alcohol, this would lead to a decrease in diastereoselectivity. Hence it can be assumed that another of the mentioned properties, concerning the nucleophilicity of benzyl alcohol, gains more influence.

Using benzoic acid as nucleophile led only to traces of the product, which were not isolated.

It was also attempted to use thiophenol and several nitrogen nucleophiles such as *n*-butyl amine, benzyl amine, *N*-methylbenzyl amine, sodium azide and trimethylsilyl azide in different solvents. However, the only successful reaction occurred with trimethylsilyl azide ($TMSN_3$) as nucleophile in dichloromethane as solvent (**114**, Table 3.4, entry 7), which resulted in 35% yield and a diastereomeric ratio of 6:1. Employing other nitrogen or sulfur nucleophiles resulted either in the recovery of starting material or led to complex reaction mixtures, which were not investigated further.

3.3 Discussion of NMR-Spectra

In this chapter a typical set of spectra of the addition products of the selenenylation reactions will be discussed. For this purpose the crude ^1H and ^{13}C NMR spectra of **103** were chosen (alkene: styrene; nucleophile: methanol; solvent: THF).

The ^1H NMR spectrum shows several signals in between 7.73 ppm and 7.21 ppm. The integration should only show nine aromatic protons. However, the integration shows ten protons, the additional integration is resulting from the NMR solvent, chloroform, which always appears at 7.26 ppm in the

obtained spectra. The singlet at 1.15 ppm, which integrates for nine protons, belongs to the *t*-butyl group. At 3.14 ppm a singlet appears with three protons for the methoxy group.

H_C (4.28 ppm), attached to the chiral carbon atom adjacent to the methoxy group, appears as a doublet of a doublet as the proton is coupling to both protons H_A (3.00 ppm) and H_B (3.29 ppm). H_A and H_B appear as two doublets of doublets and the respective coupling constants are J_{AB} = 12.2 Hz; J_{AC} = 5.1 Hz; J_{BC} = 8.3 Hz.

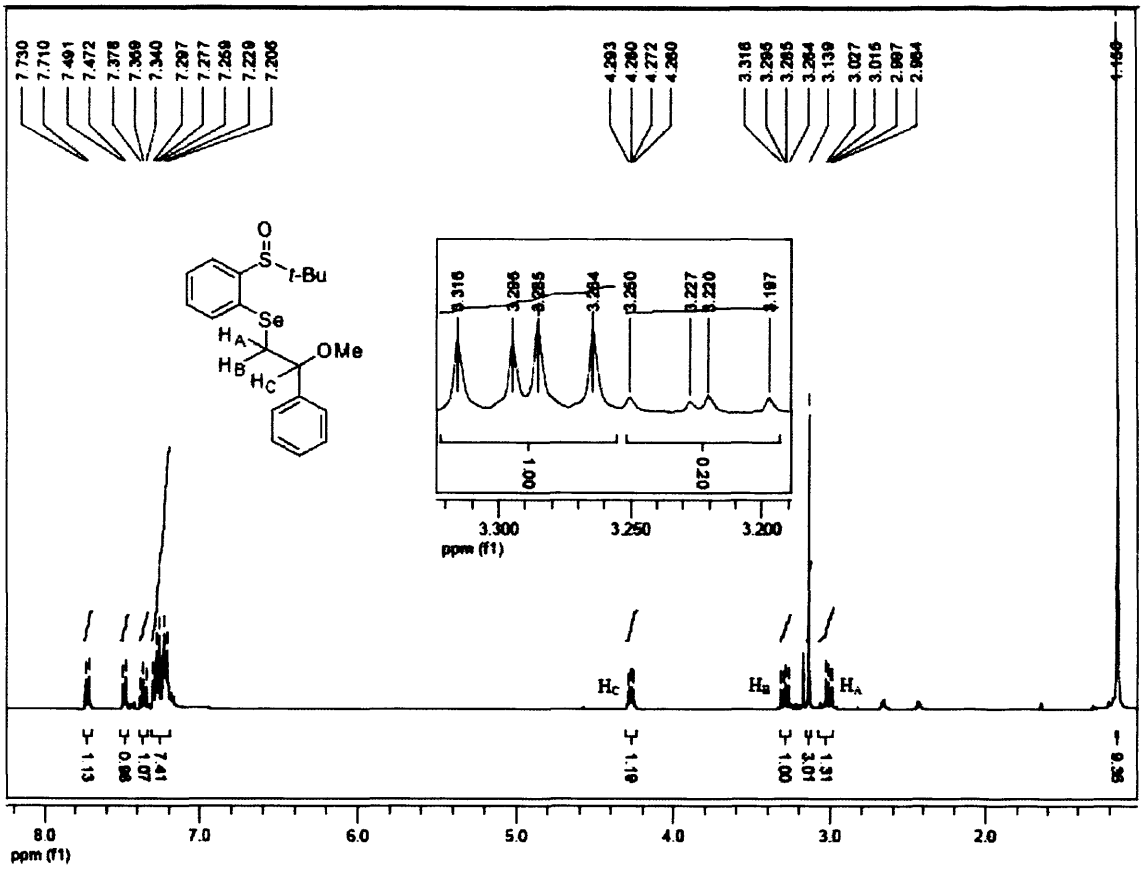


*Figure 3.3: ^1H NMR of **103** (400 MHz, $CDCl_3$)*

t is also possible to identify the minor diastereomer of compound **103** beside the doublet of doublet of H_B (enlarged section in Figure 3.3). The isomers of H_A and H_C are either partially or completely overed beneath the doublet of doublets of the major isomers. However, the ratio of the two isomers an be determined by integration of the minor and major isomer and was found to be 5:1 (enlarged ection in Figure 3.3) using THF as reaction solvent.

he minor isomer can also be seen in the carbon NMR spectrum (100 MHz, $CDCl_3$) as small peaks eside the major isomer peaks of most of the ten aromatic as well as all of the aliphatic peaks. At 3.3 ppm are the three methyl groups of the *t*-butyl group. The methoxy group and the quaternary rbon atom of the *t*-butyl group appear at 56.9 ppm and 58.2 ppm. The α-carbon atom (1) $SeCH_2CH$ ppears at 37.1 ppm and the chiral carbon atom (2) *C*HOMe appears at 82.7 ppm. Similar to the proton

NMR spectrum, the diastereomeric ratio of the two isomers can also be determined by integration of the peaks representing the chiral carbon atom (2) in the ^{13}C NMR. This is highlighted in the enlarged section in Figure 3.4, showing the two integrals for the isomeric peaks at 82.7 ppm. The ratio of the two isomers in this case is the same as in the ^{1}H NMR, confirming a diastereomeric ratio of 5:1.

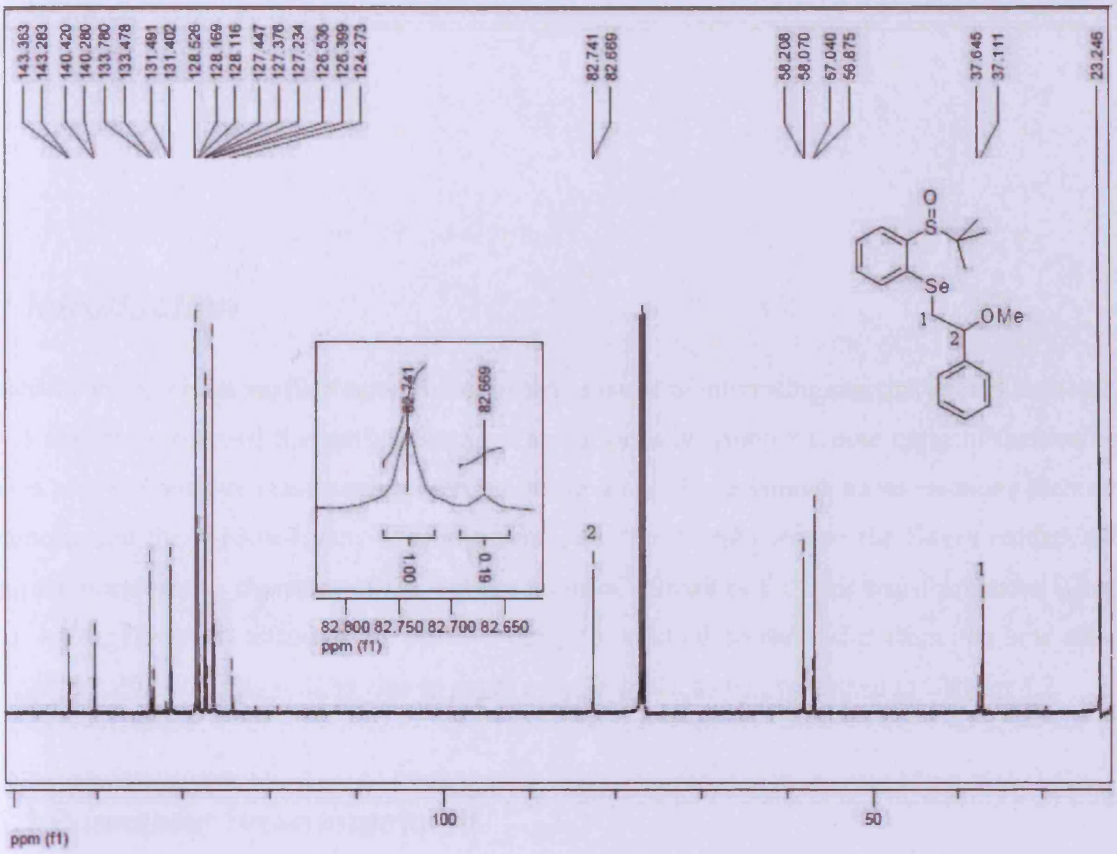


*Figure 3.4: ^{13}C NMR of **103** (100 MHz, $CDCl_3$)*

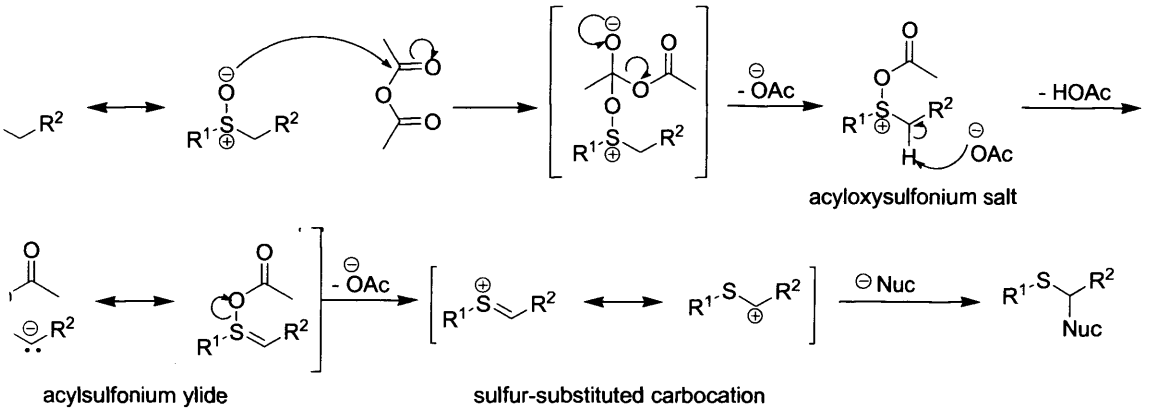
4. Cyclisation Reactions

.1 Introduction

ɔside the use as chiral auxiliaries, sulfoxides show a range of interesting reactivities. In Chapter 2.2.2 was already mentioned that sulfoxides have a significantly stronger dipole moment than carbonyl ɔups with the positive charge centred on the sulfur atom. Some famous name reactions such as the mmerer and the Mislow-Evans rearrangements, and the Kornblum and the Swern oxidations are ng the nucleophilic character of the oxygen atom of sulfoxides for their transformations (Chapter .1–4.1.4). However, although the positive charge is centred on the sulfur atom, the lone electron r on the sulfur could as well be able to act as a nucleophile, as will be shown in Chapter 4.2.

.1 Pummerer Rearrangement

909, Pummerer found that upon heating of phenylsulfinylacetic acid with strong mineral acids ı as H_2SO_4 or HCl, the formation of thiophenol and glyoxylic acid occurred.[91]

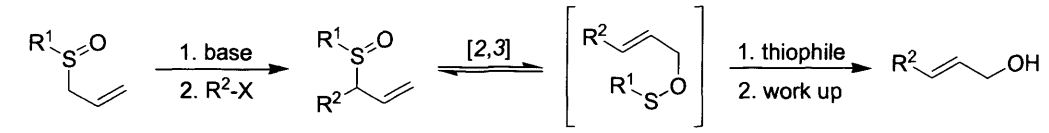


ıe 4.1: Mechanism of the Pummerer rearrangement

It was observed that the synthesis of α-substituted sulfides from the corresponding sulfoxides was a general reaction pathway, which was soon named the Pummerer rearrangement after its discoverer. As shown in Scheme 4.1, the reaction proceeds via a four-step mechanism. Firstly, the oxygen of the sulfoxide is acylated by acetic anhydride, which is the most widely used activating reagent for this rearrangement and normally added as a co-solvent. The acyloxysulfonium salt is then deprotonated in α-position by one equivalent of acetate which affords an acylsulfonium ylide. Subsequent cleavage of the sulfur-oxygen bond affords a sulfur-substituted carbocation that is captured by a nucleophile and leads to an α-substituted sulfide.

4.1.2 Mislow-Evans Rearrangement

In 1968, Mislow discovered the thermal racemisation of allylic sulfoxides.[92] Only three years later Evans[93] reported the reversible conversion of allylic alcohols to allylic sulfoxides, based on Mislow's results. The [2,3]-sigmatropic rearrangement can be used for the stereoselective synthesis of allylic alcohols from sulfoxides (Scheme 4.2).



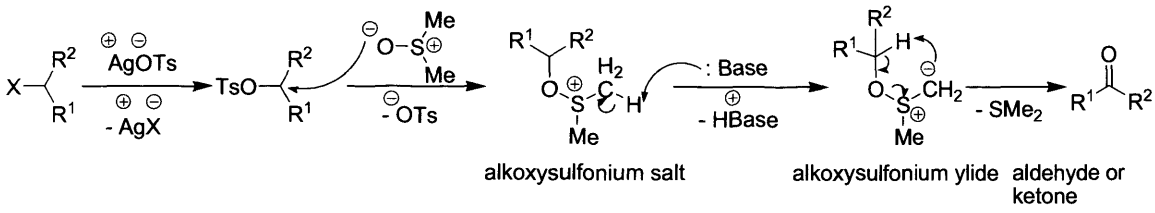
Scheme 4.2: *The Mislow-Evans rearrangement*

4.1.3 Kornblum Oxidation

Twenty years prior to Swern's report of an oxidative method using DMSO, Kornblum had already discovered that primary benzyl bromides and α-bromo aromatic ketones are oxidised to the corresponding aldehydes and phenylglyoxals, employing DMSO as solvent for the substrates.[94] In 1959, Kornblum was able to improve this reaction by broadening the substrate scope to primary and secondary alkyl halides by *in situ* displacement of the halide atom with a tosylate.[95] Today, the use of dimethyl sulfoxide as oxidising reagent for alkyl halides to obtain the corresponding carbonyl compounds is known as the Kornblum oxidation.

After the displacement of the halide with a tosylate, the mechanism proceeds via a S_N2 displacement of the tosylate by the nucleophilic oxygen atom of DMSO (Scheme 4.3). The newly formed alkoxysulfonium salt is deprotonated to generate the corresponding ylide. Finally, the ylide

decomposes to dimethyl sulfide and the desired aldehyde or ketone, by β-elimination through a five-membered cyclic transition state.

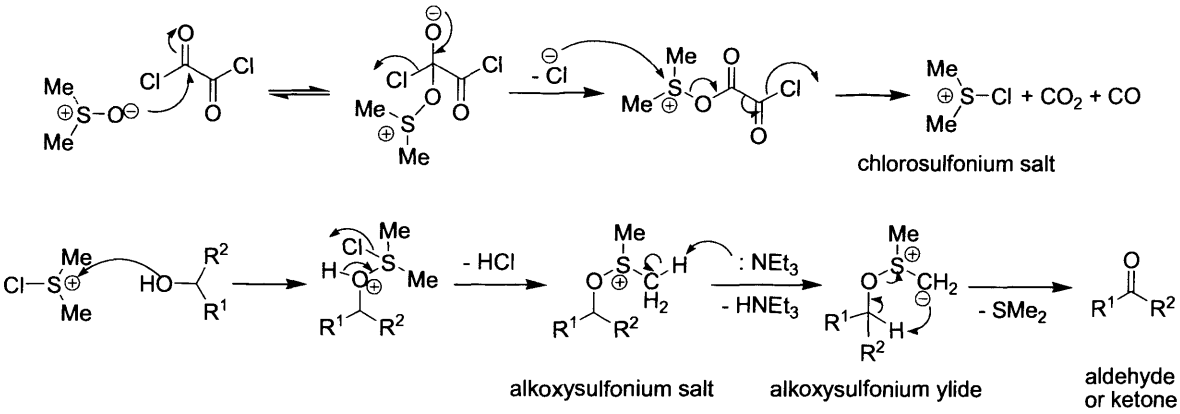


Scheme 4.3: *The Kornblum oxidation*

4.1.4 Swern Oxidation

A primary or secondary alcohol can be oxidised to an aldehyde or ketone by the Swern oxidation using oxalyl chloride, dimethyl sulfoxide (DMSO) and an organic base such as triethylamine. The reaction has a wide tolerance of functional groups, and the only by-products are dimethyl sulfide (Me_2S), carbon monoxide (CO), carbon dioxide (CO_2) and – when triethylamine is used as base – triethylammonium chloride ($Et_3N{\cdot}HCl$).

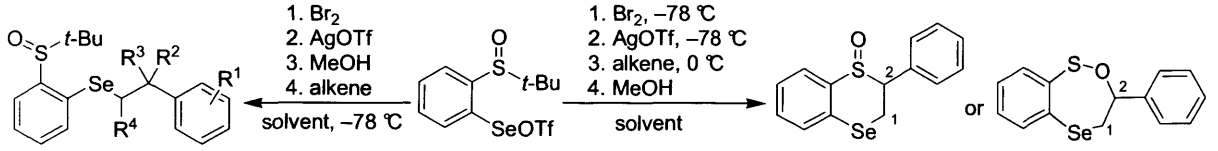
The mechanism (Scheme 4.4) starts with the attack of the nucleophilic oxygen atom of DMSO onto oxalyl chloride. The intermediate decomposes to CO_2 and CO, producing the chlorosulfonium salt. Upon addition of the alcohol, the alkoxysulfonium ion is formed which is deprotonated by the base to give the alkoxysulfonium ylide. By β-elimination through a five-membered cyclic transition state, the ylide decomposes to dimethyl sulfide and the desired aldehyde or ketone.



Scheme 4.4: *The Swern oxidation*

4.2 Cyclisation Reactions and Mechanism

The well established reaction conditions for selenenylation reactions with the new sulfoxide-containing diselenides, described in Chapter 3.2, led to the expected addition products **101** to **114**. However, when these conditions were slightly altered, the reactivity of the new selenium electrophile *rac*-**99** changed and a different product (**115** or **116**) was obtained (Scheme 4.5). For this one-pot procedure, 0.1 mmol of the diselenide was dissolved in 4 ml of solvent, cooled to −78 °C, and 100 µl of a 1 M solution of bromine in carbon tetrachloride were added to generate the selenenyl bromide. Upon addition of silver triflate and stirring for 25 minutes, the silver bromide precipitated from the solution. Then styrene was added and the mixture was warmed to 0 °C. The mixture was stirred for 20 minutes at 0 °C followed by the addition of methanol and further stirring for 2 hours at the same temperature.



Scheme 4.5: *Possible structures in accordance with NMR data*
115 *= (2,3-dihydro-1,4-benzoselenothiine-1-oxides);* ***116*** *= 1,2,5-Oxaselenathiepines*

Figures 4.1 and 4.2 show the proton and carbon NMR data of the product formed under the modified reaction conditions using selenium electrophile *rac*-**99** with styrene. In contrast to the products formed during the addition reaction (the corresponding spectra were discussed in Chapter 3.3), the methoxy group and the *t*-butyl group were missing. The styrene double bond, however, had reacted as the three vinyl protons in the proton NMR had clearly disappeared. The three signals at 3.33 ppm, 3.88 ppm and 4.51 ppm appeared as doublets of doublets showing a typical AMX three spin system with coupling constants of J_{AB} = 11.7 Hz; J_{AC} = 8.1 Hz; J_{BC} = 6.2 Hz. Additionally, only one diastereomer seemed to be present. These observations were supported by ^{13}C NMR data showing ten aromatic protons and two aliphatic protons at 16.7 ppm and 61.3 ppm. The two proposed structures, **115** and **116** (Scheme 4.5) were both in accordance with these NMR spectra.

According to Zhou *et al.*[96] there is just a small difference in the IR vibrations of a S=O double bond (998 cm^{-1}) and a S–O single bond (1014 cm^{-1}), but they can be distinguished using closely related pure reference substances. As both heterocyclic systems are not yet reported and some of the selenium related IR vibrations can be expected to be in the same region as the S=O or S–O vibrations, it was not possible to clearly identify which product had formed. Mass spectrometric data supported the existence of either one of these structures.

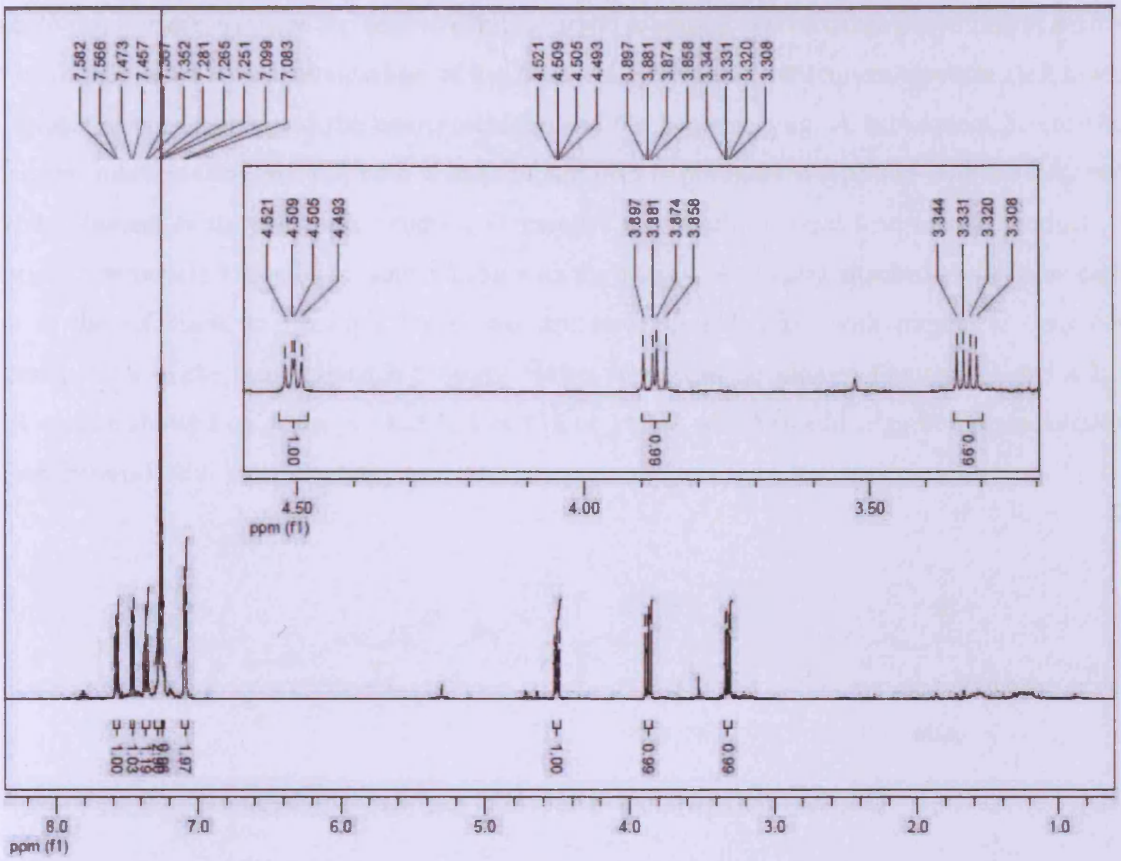


Figure 4.1: *^{1}H NMR of the new product **115** or **116** (500 MHz, $CDCl_3$)*

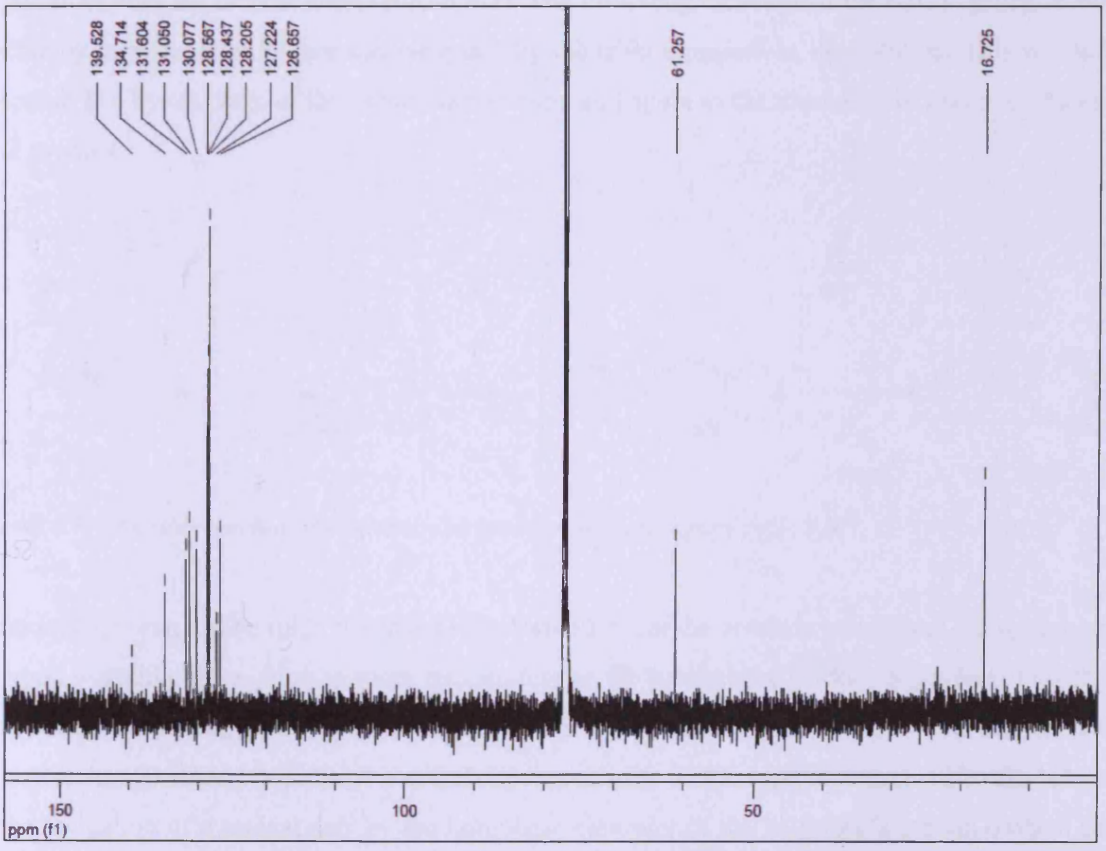
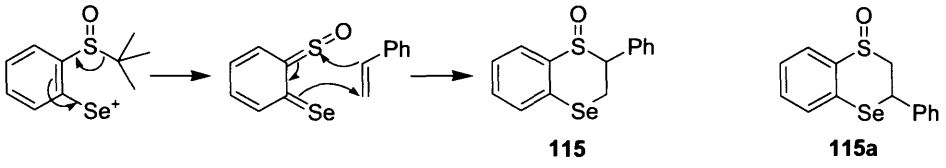


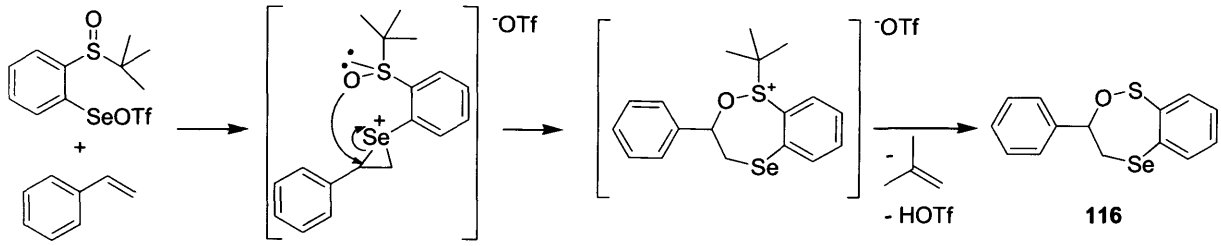
Figure 4.2: *^{13}C NMR of the new product **115** or **116** (100 MHz, $CDCl_3$)*

Possible reaction mechanisms for both structures can be proposed. The six-membered ring system **115** can be formed upon an initial cleavage of the *t*-butyl moiety and a subsequent electron shift towards the selenium atom leading to the dearomatisation of the benzene ring. A subsequent hetero-Diels-Alder type reaction (Scheme 4.6) with styrene would lead to products of type **115** with the very stable gaseous *i*-butene as the only side product. Generally, this reaction could lead to two products, the proposed heterocycle **115** and the isomer **115a** with the phenyl substituent attached to the same carbon atom as the selenium. In principle these two structures should differ with respect to their NMR chemical shifts of the three aliphatic protons. However, as can be seen in Figures 4.1 and 4.2, the NMR spectra showed only one product (either **115** or **115a**), which would suggest a regiochemically uniform hetero-Diels-Alder reaction.



Scheme 4.6: *A possible mechanistic pathway to the six-membered heterocycle **115***

The seven-membered heterocycle **116** could be formed upon attack of the lone electron pair of the oxygen atom onto the carbocation (Scheme 4.7). The following cleavage of the *t*-butyl group would be possible by deprotonation of one methyl group by the triflate present in the solution. This would lead to product **116** by cleavage of the sulfur-carbon bond and again to the formation of gaseous *i*-butene as a side product.

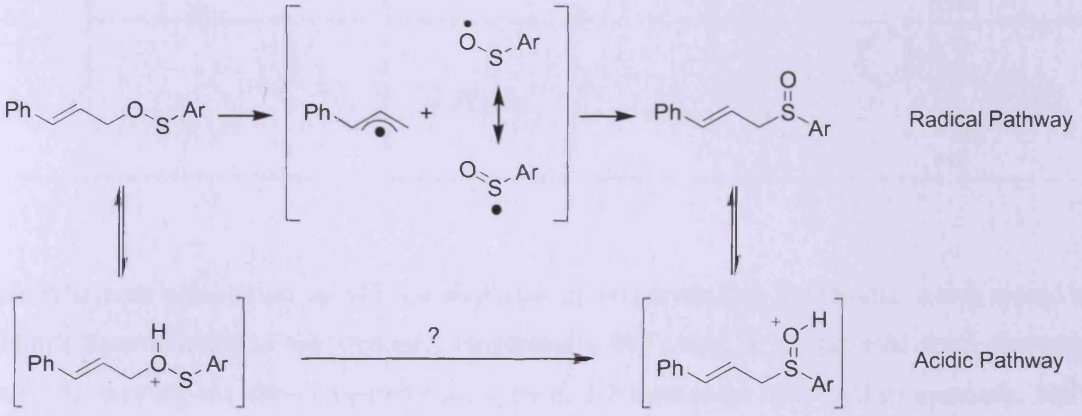


Scheme 4.7: *Possible mechanistic pathway to seven-membered heterocycle **116***

Additionally, it can not be ruled out that **116** is formed under the reaction conditions but rearranges to **115** upon warming the mixture to room temperature or the subsequent workup procedure. This theory is supported by a publication of Amaudrut and Wiest[97] (Scheme 4.8). It was found that reversible thermal rearrangements of cinnamyl-4-nitrobenzenesulfenate to the corresponding sulfoxide can occur via the formation of a radical pair by the homolytic cleavage of the sulfenate's carbon-oxygen bond. The cinnamyl group is not prone to undergo the [2,3]-sigmatropic rearrangement described in the

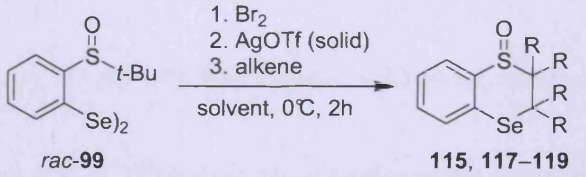
Mislow-Evans rearrangement (Chapter 4.1.2). When the reaction was performed using acetonitrile, which is a slightly acidic reaction medium, the results suggested that a competing acidic pathway is possible (Scheme 4.8). The details of this acidic mechanism, proceeding via the protonated intermediate to form the sulfoxide, remained unclear.

It is considered unlikely that a rearrangement of **116** or **115** proceeds through a radical pathway because it can be assumed that during a radical rearrangement the selenium atom would be likewise involved due to its higher reactivity towards radicals compared to sulfur or carbon. It can be expected that this high reactivity of the selenium atom would lead to more complex products. An acidic pathway towards **115** would seem more likely and indeed possible prior to the workup procedure, as triflic acid was present in the reaction mixture.



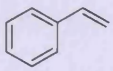
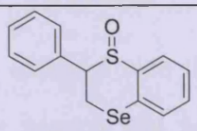
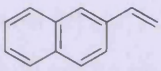
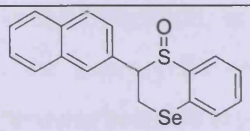
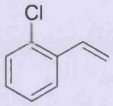
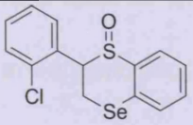
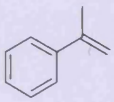
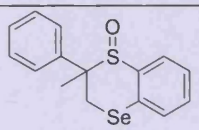
Scheme 4.8: *Thermolysis of cinnamyl-4-nitrobenzenesulfenate in acetonitrile by Wiest et al.*

To confirm the general reproducibility of this kind of reaction, further experiments with styrene were undertaken. In the beginning, the mixture was only stirred for 15 minutes at 0 °C followed by the addition of methanol, as it was believed to be crucial for the reaction mechanism. The product was obtained in 10% yield. However, the same product was also formed when no methanol at all was added. If methanol was added after 10 minutes stirring at 0 °C, some conventional addition product (**101**) was obtained as well. Addition of methanol after 20 to 30 minutes after warming the reaction mixture to 0 °C afforded only the heterocyclic product, which suggested that the reaction occured relatively fast. It was possible to the isolate starting materials along with the product and some minor side products, which were not further identified. Then different styrene derivatives were tested (Scheme 4.9 and Table 4.1).



Scheme 4.9: *Cyclisation reaction to (2,3-dihydro-1,4-benzoselenothiine-1-oxides)*

***Table 4.1**: Cyclisation reaction with different substrates*

Entry	Alkene	Solvent	Yield [%]	Product
1		THF	10	 **115**
2		THF	16	 **117**
3		Et_2O	9	 **118**
4		CH_2Cl_2	12	 **119**

2-Naphthylstyrene was chosen, as **117** was expected to be a crystalline compound, which would allow the definite determination of the structure. Fortunately, **117** could be crystallised from diethyl ether (Figure 4.3), proving the six-membered ring system. 3-Nitrostyrene and methylcinnamate, both too unreactive in the methoxyselenenylation reaction, did also not react using the altered reaction conditions. 2-Chlorostyrene and α-methylstyrene afforded the products in similar yields as styrene, proving that *α*-substituted double bonds and *ortho*-substituted aromatic systems can undergo this reaction. *ß-Trans*-substitution on the styrene double bond however, did not afford any product. This could be due to too much strain during the cyclisation.

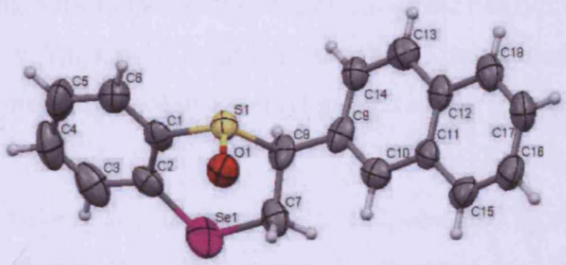


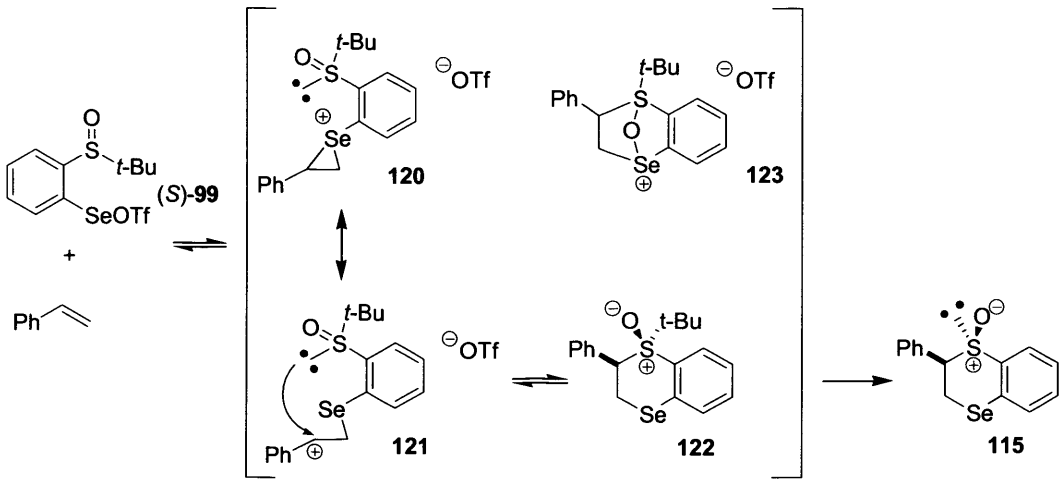
***Figure 4.3:** Crystal structure of **117** [(S*,S*)-2-Naphthyl-2,3-dihydro-1,4-benzoselenathiine-1-oxide]*

The crystal structure (Figure 4.3) of **117** proved the presence of the six-membered heteroyclic system with a sulfoxide moiety. Remarkably, according to this crystal structure, the oxygen atom and the

naphthyl ring system are on the same side of the newly formed heterocycle which indicates that the cleavage of the *t*-butyl group occurs after the sulfur-carbon bond formation.

Furthermore, it supports the observed optical rotation of the product **115** obtained with the non-racemic selenenyltriflate (*S*)-**99** ($[\alpha]_D^{20} = -48$). These two results strongly suggest that neither a hetero-Diels-Alder type reaction nor a rearrangement occur during the product formation, as both reactions would most likely lead to products with *anti*-configuration on the heterocyclic system. Additionally, it would not be possible to observe any optical activity as the products could be expected to be racemic.

Therefore the proposed mechanistic pathway shown in Scheme 4.10 seems to be reasonable for the formation of **115**.

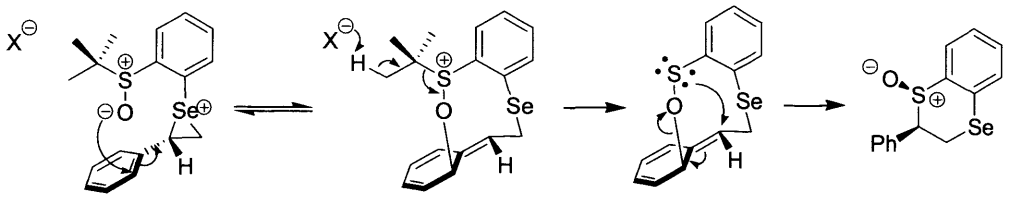


Scheme 4.10: *Proposed mechanistic pathway*

Seleniranium cation **120** is in resonance with carbocation **121**. After the formation of cation **120/121**, the lone electron pair on the sulfur atom attacks the electrophilic benzylic carbon atom in **121** to form intermediate **122** selectively. The newly formed six-membered ring-system is stabilized upon cleavage of the *t*-butyl group by deprotonation of one methyl group to form the very stable gaseous *i*-butene as a side product.

Calculations by Michio Iwaoka of similar structures as **122**, obtained by replacing the *t*-butyl group by a methyl group, have shown that an oxygen involvement as found in intermediate **123** ($\Delta E = +8.264$ kcal/mol) is unlikely. Because the energy calculated for this structure (**123**) is above the energy of the methyl analogue of **122** ($\Delta E = 0.000$ kcal/mol).[98,99]

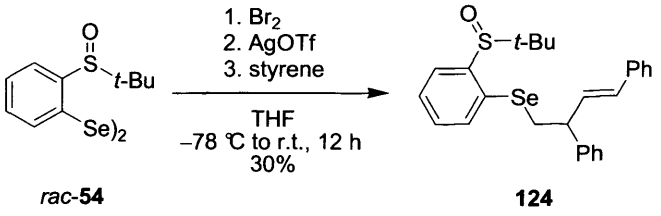
Another possible mechanism, proposed by Barry Carpenter, suggests the involvement of the styrene aromatic ring system during the product formation (Scheme 4.11).



Scheme 4.11: *Proposed mechanistic pathway by Barry Carpenter*

Initially, the oxygen atom of the sulfoxide moiety attacks the slightly electron deficient π-system of the aromatic system in *ortho*-position to the α-carbon of the seleniranium ring system. This leads to the dearomatisation of the aromatic ring and the opening of the three-membered ring. Upon cleavage of the *t*-butyl group a neutral nine-membered ring system can be generated. A following Mislow-Evans rearrangement, regenerating the aromatic system and establishing to a more stable six-membered heterocyclic system, could lead to the observed products. If this pathway would be able to lead exclusively to the observed stereochemistry was not established.

In order to improve the low yields of the cyclisation reaction, the reaction mixture was warmed to room temperature overnight without the presence of methanol. However, again a different kind of reactivity was observed under these conditions (Scheme 4.12). If styrene was present in excess, dimer **124** was formed in a 1:1 diastereomeric mixture with 30% yield. The formation of the dimer proceeds via a cationic dimerisation reaction and regenerates the double bond by deprotonation during the workup. Although this reaction was also attempted with diphenyl diselenide, it only afforded a statistical mixture of polymerised products which were not further identified. The steric bulk of the *t*-butyl group is most likely the reason for the controlled formation of the dimer, as it could shield the intermediate carbocation from further attack.

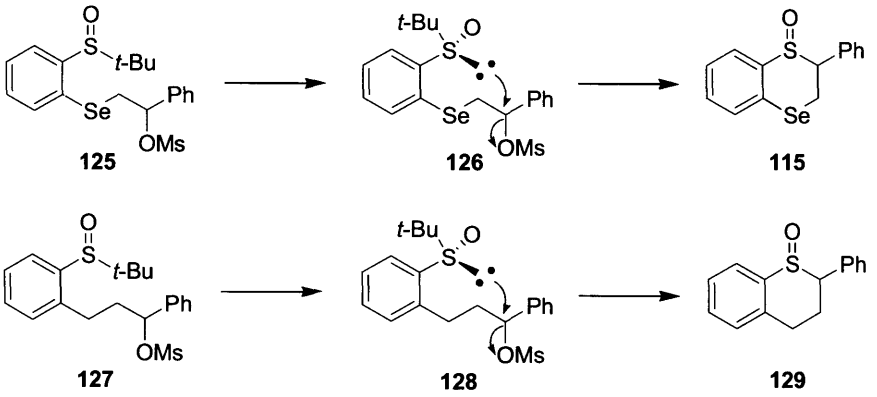


rac-**54** **124**

Scheme 4.12: *Formation of dimer* ***124*** *with styrene acting as nucleophile*

One of the reasons for the low yield during the cyclisation reaction could be the occurring resonance between seleniranium cation **120** and carbocation **121**. If it were possible to shift the resonance in favour of the carbocation and ensure the cleavage of the *t*-butyl group, the reaction could proceed with higher yields.

In order to test this hypothesis it could be worthwhile to synthesise compound **125** (Scheme 4.13), which in principle could follow the reaction mechanism proposed in Scheme 4.10.



Scheme 4.13: *Alternative synthesis of **115** and analogue reaction pathway to **129***

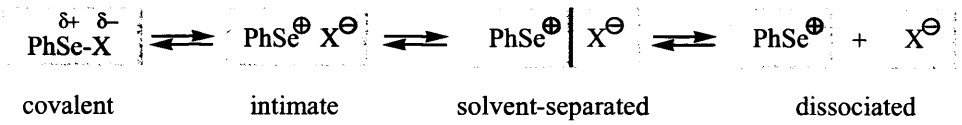
If this starting material (**125**) would afford the proposed product **115,** the yield should be improved. Additionally, the analogue **127** as starting material should lead to a similar structure **129**, assuming that the reactivity of the sulfoxide is consistent. Unfortunately, this idea could not be tested within the scope of this thesis.

5. Chiral Counteranions in Selenenylation Reactions

In this chapter, research concerning the influence of chiral couteranions on electrophilic selenium species ($PhSe^+$) is presented. First, general aspects on the reactivity depending on the solvent and the counterion will be discussed. Then some examples for the concept of "Asymmetric Counteranion Directed Catalysis" (ACDC) will be given, showing the successful manipulation of reactions using cationic intermediates with anionic counterions. The chapter will conclude highlighting the results on the current research combining typical selenenylation reactions and the ACDC concept.

5.1 Effects on the Se–Anion Bond in Electrophilic Selenium Species in Solution

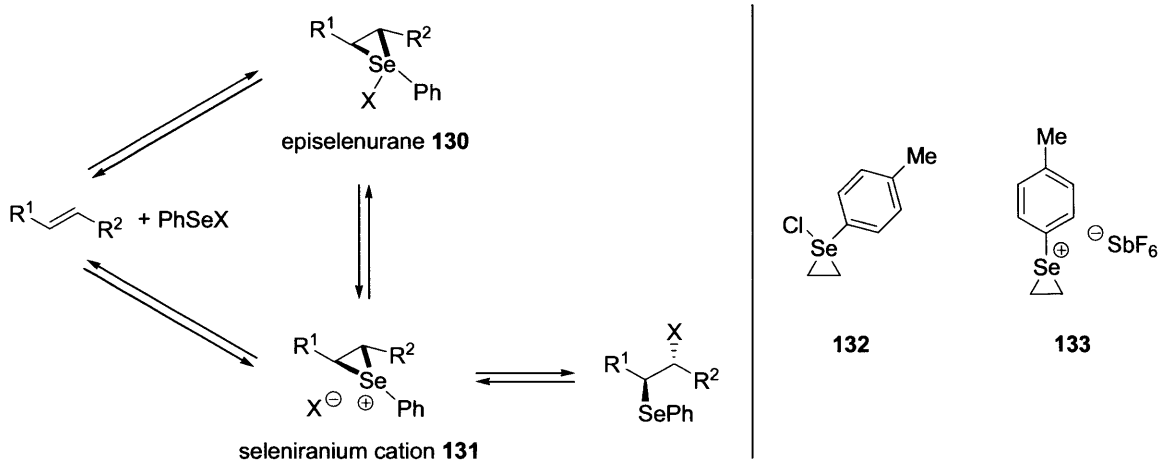
The nature of the selenium–counterion bond in phenylselenenyl species and their counterions is not yet fully understood. Generally, there are several possibilities for the interaction between the selenium and its counteranion X^-. As was already mentioned in Chapter 3.1, X^- can be any halide ion or anions like triflate,[74] hexafluorophosphate,[76] hexafluoroantimonate,[76] tolylsulfonate[77] and bistrifluoroacetate[82]. The selenium–X^- bond can be either covalent or ionic. Depending on the solvent and the reaction conditions, the ionic state could appear as an intimate ion pair where jointly solvated counterions are in very close association with no solvent molecules between them. However, the ion pair can also be solvent-separated or completely dissociated (Scheme 5.1).



Scheme 5.1: *Possible structures of PhSe-X in solution*

The same assessment concerning covalent bonding or ion pairing can be made in respect of episelenuranes **130** and seleniranium cations **131** (Scheme 5.2). Both species (**132** and **133**) were

isolated and characterised by Garratt and Schmidt.[100] However, especially episelenuranes seem to be rather rare and were so far only observed with chlorine (**132**). According to unpublished NMR experiments conducted by Santi and co-workers, the Se–Cl bond of phenylselenenyl chloride, a covalently bonded solid reagent, does not dissociate in methanol and the Se–Cl bond is also stable after the attack of the positively charged selenium atom onto the styrene double bond. So far, no such studies were done using the highly moisture-sensitive phenylselenenyl triflate, but it can be assumed that triflate as a non-nucleophilic counterion is most likely to form a seleniranium-triflate ion pair.

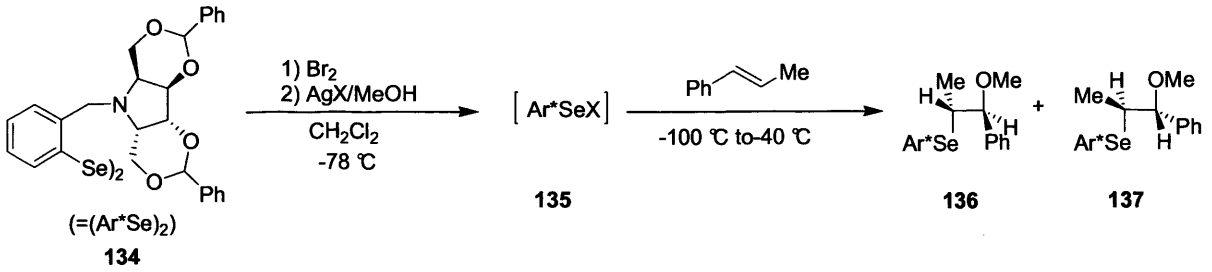


Scheme 5.2: *Structures of episelenuranes and seleniranium cations*

5.2 Counteranion-Effects on Reactions with Electrophilic Selenium

In Chapter 3.1 it was mentioned already that some electrophilic selenium reagents are commercially available, such as PhSeCl and PhSeBr. However, most selenium electrophiles are generated *in situ* by treatment of the corresponding diselenides with chlorine, sulfuryl chloride or bromine. Addition reactions with these reagents can be problematic as the halide anions compete with other external nucleophiles or during cyclisation reactions, which leads to undesired side products and a decrease in selectivity. They can be replaced with the less nucleophilic anions like triflate, sulfate, perchlorate, tetrafluoroborane and hexafluorophosphonate by treating the selenium electrophile with the appropriate silver salt.

The effect of the counteranions on the course of these reactions was investigated by Tomoda *et al.*[101], Tiecco and co-workers[102] and Khokhar and Wirth[103]. On the basis of these results it was suggested that a decrease in the nucleophilicity of the counteranion, i.e. an increase in the electrophilicity of the selenium reagent, produces an enhancement of the diastereomeric excess of the reactions.



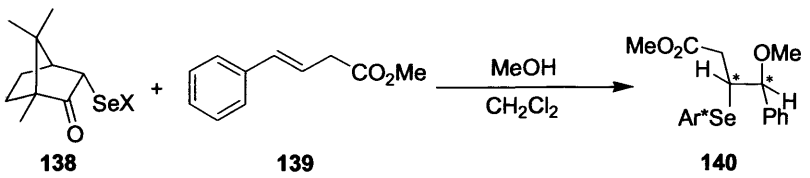
Scheme 5.3: *Tomoda's test reaction using different counteranions*

Table 5.1: *Tomoda's results using different counteranions*

X^-	Yield [%]	136:137	*d.e.* [%]
Br^-	85	3.2:1	52
ClO_4^-	47	9:1	80
$CF_3O_2SO^-$	68	17:1	89
BF_4^-	67	18:1	90
SbF_6^-	64	31:1	94
PF_6^-	58	37:1	95

Tomoda[99] found that various selenoesters **135** showed a significant enhancement in the diastereomeric excess (*d.e.*) during the methoxyselenenylation of *β*-methylstyrene at –100 °C to –40 °C (Scheme 5.3, Table 5.1). Using perchlorate as anion improved the *d.e.* to 80%, compared to the corresponding selenenyl bromide (52% *d.e.*). The selenohexafluorophosphate gave the highest selectivity (95% *d.e.*).

Camphorselenenyl reagents **138** were employed by Tiecco and co-workers in the methoxyselenenylation of methyl styrylacetate **139** (Scheme 5.4, Table 5.2).[100]



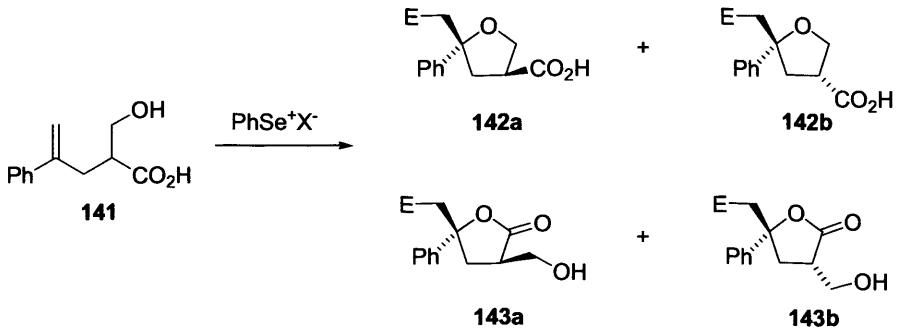
Scheme 5.4: *Tiecco's test reaction using different counteranions*

Table 5.2: *Tiecco's results using different counteranions*

X^-	T [°C]	t [h]	Yield [%]	*d.r.*
Cl^-	0	4	49	40:60
Br^-	0	2	59	35:65
$CF_3O_2SO^-$	0	5	77	42:58
OSO_3H^-	25	24	94	85:15

Selenenyl chloride and bromide led to low yields (49% and 59%) and poor diastereoselectivities (40:60 and 35:65). The use of camphorselenenyl triflate improved the yield to 77%, but the diastereomeric ratio had barely improved (42:58). They observed no significant change in yields or selectivities when the reactions were run at 0 °C or at –30 °C with these reagents. However, when camphorselenenyl sulfate was employed at room temperature for 24 h, the diastereomeric ratio improved to 85:15 and the yield rose to 94%. Another observation was that the addition using the sulfate anion occurs with a facial selectivity different from that observed previously.

Khokhar and Wirth synthesised alkene **141**, which contained two competing nucleophiles (alcohol and carboxylic acid), to probe the effect of different counteranions on the selenocyclisation reaction (Scheme 5.5, Table 5.3).[101]



***Scheme 5.5:** Wirth's electrophilic cyclisation of **141** to tetrahydrofuranes **142** and lactones **143** with different counteranions*

***Table 5.3:** Wirth's results using different counteranions[a]*

X^-	**142a/142b**	**143a/143b**	**142/143**	Yield [%]
$CF_3O_2SO^-$	13:87	81:19	63:37	67
BF_4^-	0:100	84:16	14:86	70
PF_6^-	-	78:22	0:100	50
PF_6^{-} [b]	0:100	73:27	30:70	85
SO_4^{2-} [c]	-	67:33	0:100	42

[a] Standard reaction conditions: Diethyl ether, 2.5 h, 10 equiv. methanol, – 78 °C; [b] Reaction time 5.5 h; [c] Slow reaction due to insolubility of Ag_2SO_4, 40% starting material recovered.

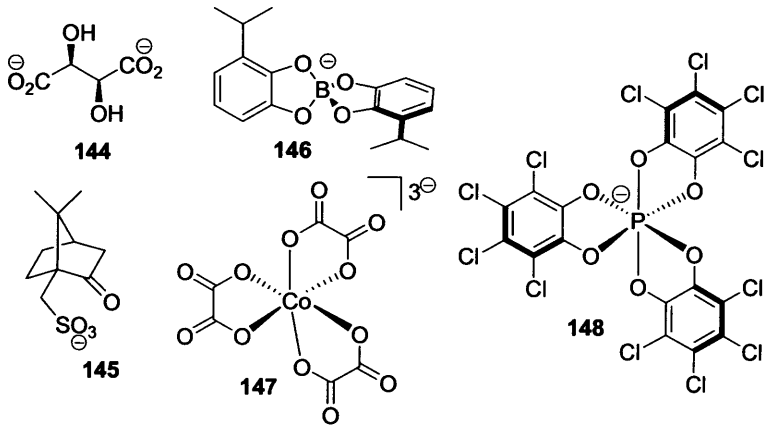
Whereas phenylselenenyl triflate and tetrafluoroborate gave mixtures of tetrahydrofuranes **142** and lactones **143**, the corresponding hexafluorophosphate and sulfate generated exclusively lactones **143** (Table 5.3). When the reaction time was extended to 5.5 h using hexafluorophosphate the formation of small amounts of tetrahydrofurane **142b** was observed.

These examples show that the counterion indeed has an influence on the selectivities of selenenylation reactions. Therefore it seemed to be viable to combine these observations with the concept of the "Asymmetric Counteranion Directed Catalysis" (ACDC).

5.3 Asymmetric Counteranion Directed Catalysis (ACDC)

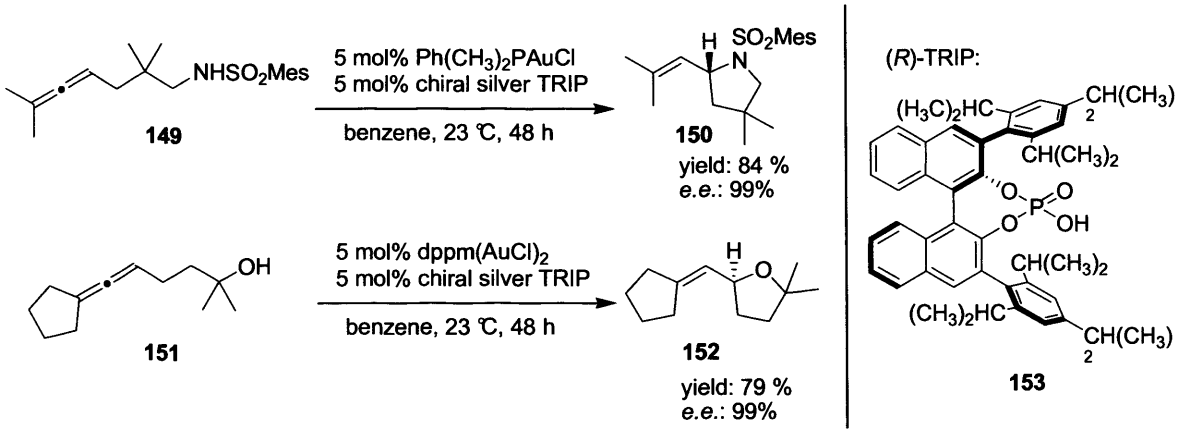
The concept of "Asymmetric Counteranion Directed Catalysis" (ACDC) is a relatively new development which emerged in the field of organocatalysis.[5] Reactions proceeding *via* anionic intermediates have been successfully influenced by chiral cationic counterions. The combination of chiral ions with enantiopure counterions can lead to two ion pairs with different stabilities and different chemical and physical properties. One ion pair can be formed preferentially if it is more stable. This concept has already been used for racemic resolutions as well as for synthesis. It is well known that high levels of asymmetric induction can be achieved using chiral cations and achiral anions. Recently, it could also been shown that this concept works also for cationic intermediates and transition states with chiral counteranions. Several independent reports in the field of enantioselective organocatalysis have highlighted that chiral anions are also able to influence the selectivity of a reaction.

In 2003, Lacour published a review highlighting the synthesis and reactions of chiral counteranions.[104] Beside natural compounds such as chiral carboxylic **144** and sulfonic acids **145**, which possess a rather large number of potential conformations, a number of chiral metallo-organic complexes **147**, tetrahedral borates **146** and phosphate anions **148** were presented (Scheme 5.6).



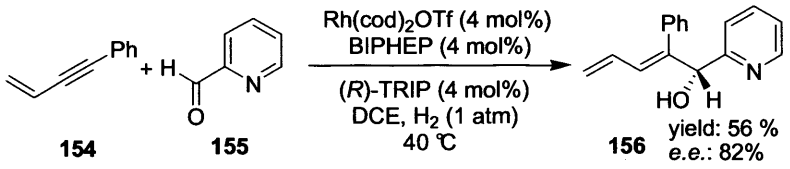
***Scheme 5.6:** Chiral counteranions proposed by Lacour*

Toste and co-workers reported in 2007 the first highly successful application of the metal-ACDC catalysis concept in a gold(I) catalyzed heteroatom cyclisation reaction of allenes.[105] High enantioselectivities with up to 99% enantiomeric excess (*e.e.*) were achieved in hydroaminations (mesylamines, **149**) and hydroalkoxylations (allenic alcohols, **151**) (Scheme 5.7). In the case of substrates that lack sterically demanding substituents and for which high enantioselectivity is therefore difficult to achieve, the chiral anion strategy remained efficient with up to 80% *e.e.* When a chiral phosphine ligand on the silver acts in synergy with the anionic counterion **153**, a higher proportion of the major enantiomer is produced (up to 92% *e.e.*).



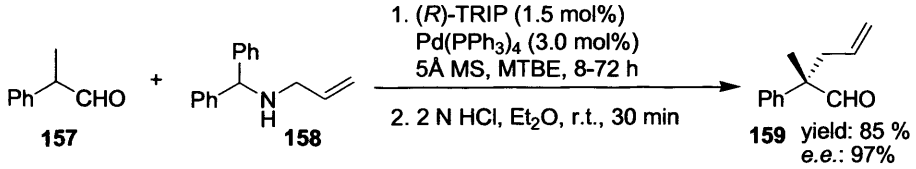
Scheme 5.7: *Counterion-mediated enantioselective hydroamination by Toste*

In 2006, Komanduri and Kirsche had already described a Rh-catalysed reductive coupling of 1,3-enynes **154** to heterocyclic aromatic carbonyl compounds **155** using chiral bisphosphine ligands to induce high enantioselectivities (Scheme 5.8).[106]



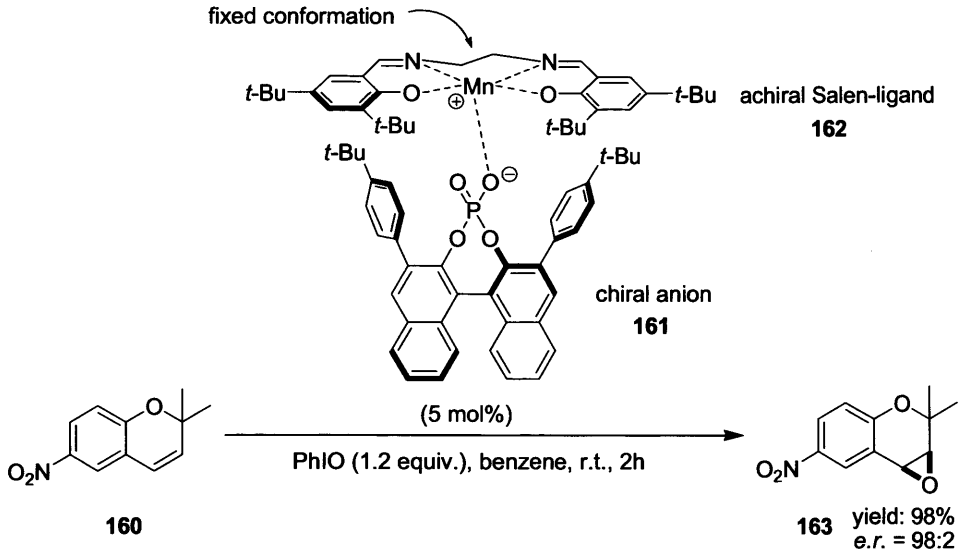
Scheme 5.8: *Rh-catalysed reductive coupling by Komanduri and Kirsche*

The group of List reported the first application of the chiral counteranion strategy for Pd-catalysed asymmetric allylic alkylations (Scheme 5.9).[107]



Scheme 5.9: *Pd-catalysed asymmetric allylic alkylation by List*

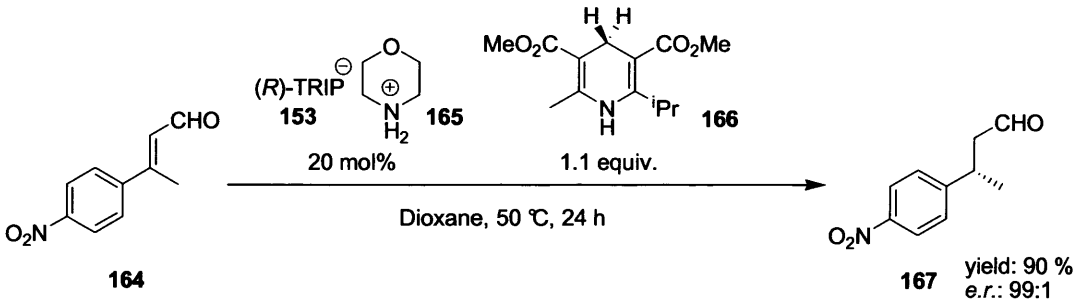
The newest development in the area of metal-ACDC is the Mn(III)-catalysed epoxidation of alkenes by Liao and List (Scheme 5.10).[108] The chiral anion **161** in the reaction mixture functions as an anchor for the enantiomorph conformation of the manganese-Salen complex **162**. The Mn(III)-complex **162** is kept in a fixed conformation throughout the reaction by the complexation of the (*S*)-BINOL-based phosphoric acid **161**.



Scheme 5.10: *Mn(III)-catalysed epoxidation of alkenes by List*

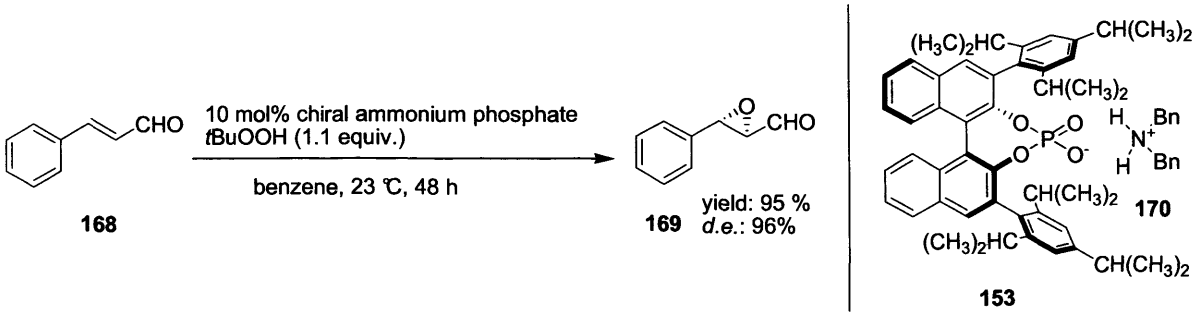
In organocatalysis, the "Asymmetric Counteranion Directed Catalysis" was also successfully applied for metal-free transfer hydrogenations of α,β-unsaturated aldehydes and ketones.[107,108] Several primary or secondary amines in combination with a chiral phosphoric acid, e.g. 3,3'-bis(2,4,6-triisopropylphenyl)- 1,1'-binaphthyl-2,2'-diylhydrogenphosphate (abbreviated as TRIP) **153,** proved to be even more successful than those which use chiral amine catalysts.

List and Mayer have shown that TRIP **153** together with secondary amine **165** can modulate the enantioselective transfer hydrogenation of α,β-unsaturated aldehydes **164** with an enantiomeric excess of up to 98% (Scheme 5.11).[109]



Scheme 5.11: *Organocatalytic transfer hydrogenation by List and Mayer*

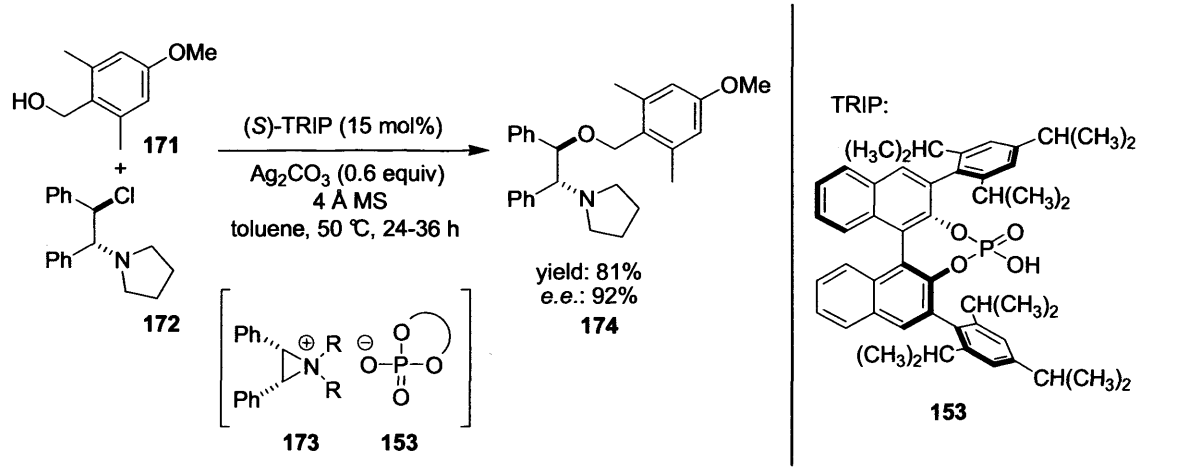
Besides the transfer hydrogenations the catalytic concept of ACDC was successfully applied for the iminium-catalysed enantioselective epoxidation of α,β-unsaturated aldehydes. List *et al.* used the same chiral counteranion **153** in asymmetric epoxidations of enals **168** with similar success (Scheme 5.12).[110] The reaction produced product **169** with up to 95% yield and 96% *d.e.*



Scheme 5.12: *Iminium-catalysed enantioselective epoxidation of α,β-unsaturated aldehydes by List*

The potential of ACDC, with a special consideration of the work planned in this thesis, has recently been demonstrated by the research group of Toste in two different asymmetric transformations. In all these cases the phosphate anion TRIP has been used to induce stereoselectivity.

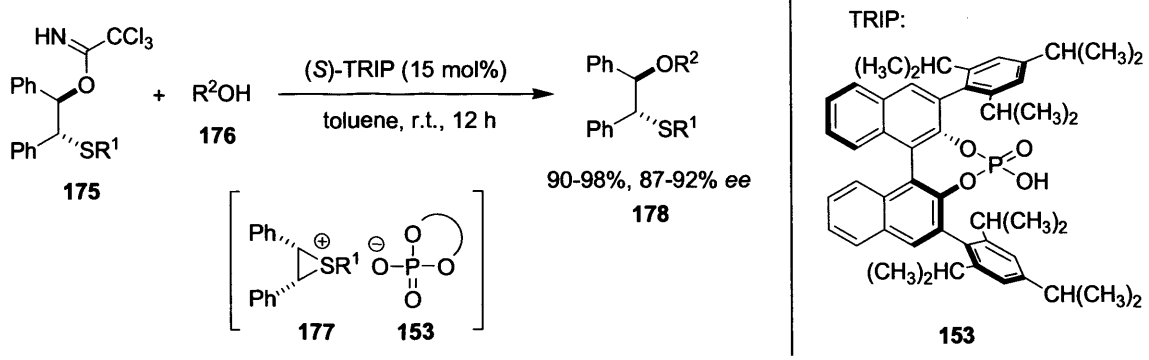
Toste and co-workers successfully demonstrated an enantioselective synthesis of β-alkoxy amines **174** from racemic β-chloro tertiary amines **172** and alcohols **171** as an oxygen nucleophile under the influence of an equimolar amount of silver(I) salt and a catalytic amount of chiral phosphoric acid **153** (Scheme 5.13).[111]



Scheme 5.13: *Enantioselective synthesis of β-alkoxy amines by Toste*

The reaction proceeds via the asymmetric ring opening of intermediary *meso*-aziridinium ions (**173**) that were generated from the ring closure of β-chloro tertiary amines (**172**) by silver(I) salts. Subsequent nucleophilic ring opening of *meso*-aziridinium ions **173** by alcohols **171** provided the corresponding β-alkoxy amines (**174**). Secondary, tertiary, and relatively hindered primary alcohols could be used in the reaction, giving β-alkoxy amines with high enantioselectivities. The efficient desymmetrization of the *meso*-aziridinium ion **173** was achieved under the influence of the chiral counteranion derived from phosphoric acid **153**. It is pointed out that the resulting catalytic process can be regarded as chiral anion phase-transfer catalysis in analogy to the established chiral cation alternative.

Toste and co-workers further extended their chemistry to the sulfur analogue of the ring opening reaction, the desymmetrization of *meso*-episulfonium ions **177** (Scheme 5.14).[109]



Scheme 5.14: *Enantioselective synthesis of β-alkoxy sufides by Toste*

However, in this application the silver–halogen abstraction method for the generation of the cationic intermediate could not be utilized because the sulfide would likely bind silver(I). Therefore, they employed trichloroacetimidate as the leaving group. The trichloroacetimidate moiety is directly activated by chiral phosphoric acid **153**, and this is followed by ring closure with concomitant loss of trichloroacetamide from substrates **175** generating ion pairs of *meso*-episulfonium ions **177** and the chiral counteranion. The interception of intermediate **177** with an oxygen nucleophile, such as alcohols **176**, affords chiral sulfide products **178** in excellent yields with good enantioselectivities.

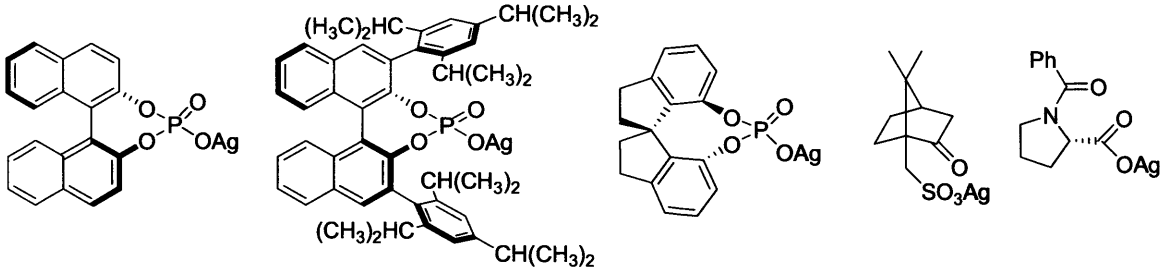
In the light especially of the last example it is anticipated that a combination of a selenenylating reagent and a chiral counteranion leads to improved selectivities in selenenylation reactions, considering the occurrence of the seleniranium intermediate in these reactions.

5.4 Synthesis of Chiral Counteranions

The counteranion effects on the enantioselectivity of selenenylation reactions shown in Chapter 5.2 and the synthesis and use of chiral counteranions using the ACDC concept (Chapter 5.3) seems to be a promising tool to enhance the diastereoselectivity of selenenylation reactions. Several silver salts (Scheme 5.15) were planned as chiral anionic reagents for the selenenylation reactions of alkenes.

BINOL derivatives have proven to be effective in several asymmetric counteranion-mediated reactions. A tool to enhance the rigidity of the backbone is the introduction of large substituents at 3,3'-positions or 6,6'-positions on the BINOL scaffold. In this case, the synthetic efforts were concentrated on the 3,3'-positions. The corresponding phosphoric acids of silver salts **179** and **180** are commercially available but costly if purchased enantiomerically pure. Initially, these reagents were

needed in stoichiometric amounts for the selenenylation reactions it was decided to synthesise both BINOL-phosphoric acid (BINOL-P) derivatives within the course of this thesis. The more rigid backbone of SPINOL phosphoric acids (SPINOL-P) and its silver salt **181** could be interesting, as the rigidity of BINOL-P derivatives can be mimicked without the steric bulk at the 3,3'-positions. Additionally, the silver salts of camphorsulfonic acid **182** and prolin derivative **183** were synthesised from easily accessible natural products from the "chiral pool" (camphor and proline). Both starting materials are cheap, and especially prolin derivatives have already proven to be successful organocatalysts.

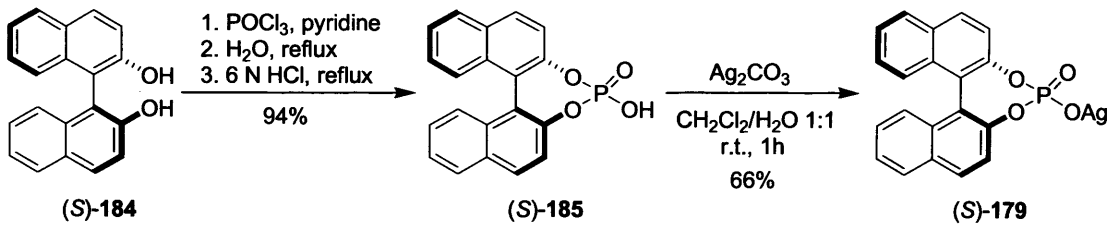


(*S*)-**179** (*S*)-**180** (*R*)-**181** (*S*)-**182** (*S*)-**183**

Scheme 5.15: *Proposed chiral silver salts as counteranions for electrophilic selenium*

5.4.1 Synthesis of Phosphoric Acids with a Binaphthyl Scaffold

The BINOL backbone is today commonly used as scaffold in enantioselective metal catalysed reactions; however, it was established in 1979 by Noyori and co-workers as stoichiometric ligand in the enantioselective reduction of ketones with $LiAlH_4$.[112] The high inversion barrier of 158 kJ/mol is the reason why the racemisation of the isomers is, although possible under highly acidic conditions, improbable.[113] Based on a modified procedure of Toste *et al.* (*S*)-(+)-1,1'-binaphthyl-2,2-diyl silver phosphate [(*S*)-AgBINOL-P] was derived from (*S*)-BINOL.[11] (*R*)- and (*S*)-1,1'-bi-2,2'-naphthol (**184**) were obtained by resolution of *rac*-BINOL using *N*-benzyl-cinchonidinium chloride [82% recovery of the (*S*)-enantiomer (99% *e.e.*) and 83% recovery of the (*R*)-enantiomer (99% *e.e.*)].[114]

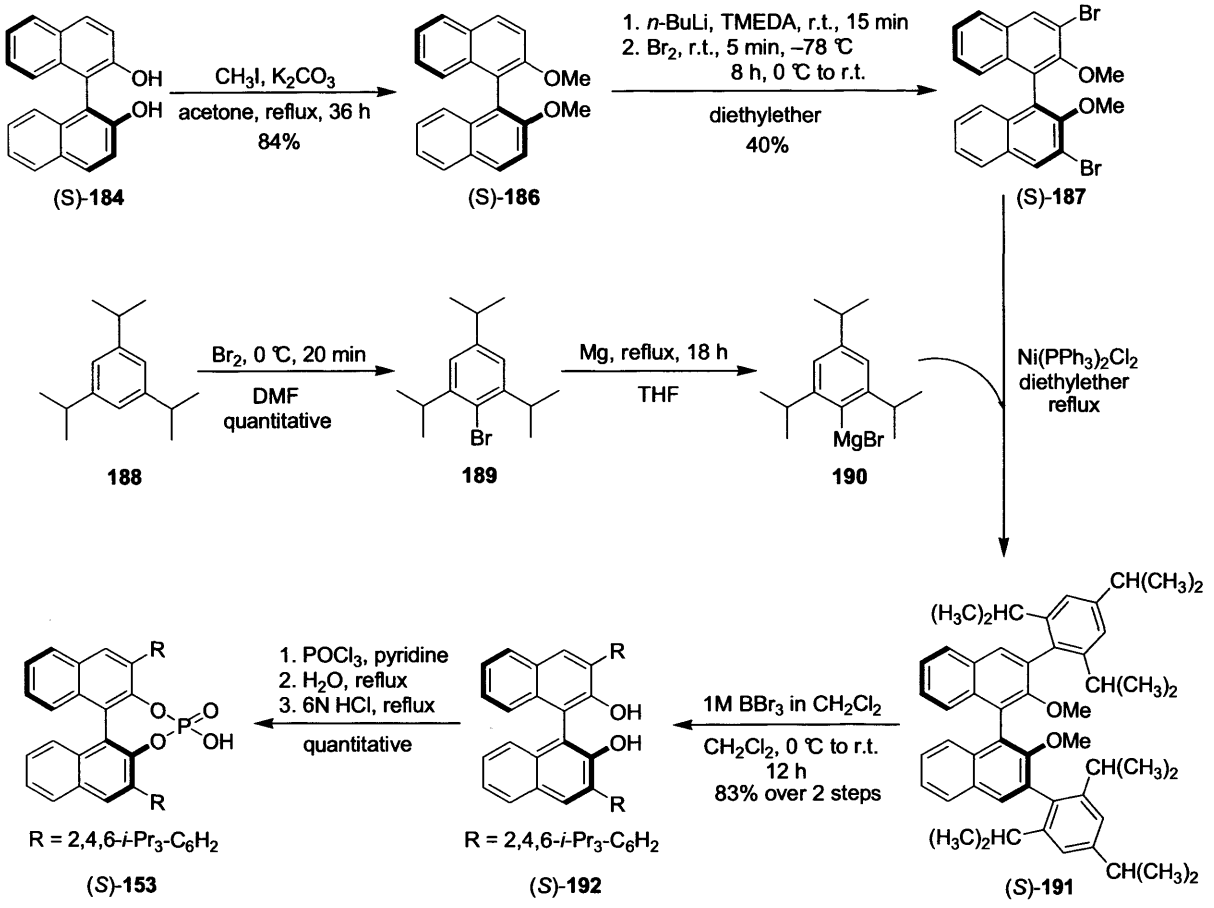


(*S*)-**184** (*S*)-**185** (*S*)-**179**

Scheme 5.16: *Chiral acids as counteranions for electrophilic selenium*

(*S*)-BINOL **184** was heated with phosphorus oxychloride and pyridine to form binaphthylphosphoric acid chloride, which was successively treated with water and hydrochloric acid to yield (*S*)-BINOL-P **185** in 94% yield (Scheme 5.16).[115] The acid was then stirred at room temperature for 1 h with silver carbonate and the resulting white silver salt (*S*)-**179** was obtained in 66% yield.

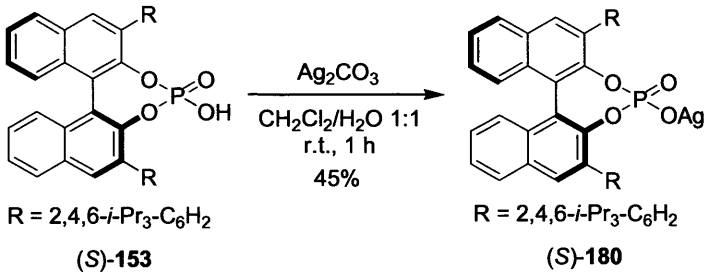
Encouraged by the good results obtained with (*R*)-TRIP **153** by several groups, it seemed to be worthwhile to employ its silver salt in the selenenylation reaction. Therefore, BINOL-scaffold **153** was synthesised via known literature procedures by Wipf and co-workers[116] and Schrock et al.[117]



***Scheme 5.17:** Synthesis of chiral phosphoric acid TRIP (153)*

Methylation of **184** with methyl iodide afforded (*R*)-**186** in 85% yield and (*S*)-**186** in 84% yield (Scheme 5.17).[114] The enantiomers were then separately treated with *n*-BuLi and TMEDA (*N,N,N',N'*-tetramethylethylenediamine) in diethylether at room temperature to generate the 3,3'-dilithiated species, which was reacted with bromine at –78 °C to afford dibromide (*S*)-**187** in 40% yield and (*R*)-**187** in 30% yield.[114] Starting material was recovered as well as some mono-brominated products. Then 2,4,6-tri(*i*-propyl)phenylmagnesium bromide **190** was prepared by stirring 2,4,6-tri(*i*-propyl)phenyl bromide **189** with magnesium in refluxing THF. Compound **189** was synthesised by the bromination of **188** in DMF in quantitative yield.[118] Brominated compounds (*S*)- and (*R*)-**187** were then used in *Kumada*-coupling reactions with Grignard reagent **190** in diethylether.[115] According to various

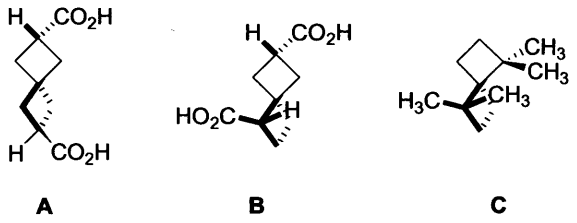
literature sources this is the most convenient method for the introduction of triisopropyl moieties in the 3,3'-positions of the BINOL scaffold. The products (*S*)- and (*R*)-**191** were used crude for the next step. The methoxy groups were deprotected with boron tribromide in dichloromethane and (*S*)-**192** was then reacted with phosphorous oxychloride in pyridine to give (*S*)-**153** [(*S*)-TRIP] in quantitative yield.[115] The hydrogen phosphate (*S*)-**152** was then converted into silver salt (*S*)-**180** [(*S*)-AgTRIP] with silver carbonate in 45% yield according to Toste's procedure (Scheme 5.18).[103]



Scheme 5.18: *Synthesis of (S)-AgTRIP*

5.4.2 Synthesis of Phosphoric Acids with a Spirobiindane Scaffold

Spiranes are bicyclic organic compounds where two aliphatic ring systems are connected through only one atom, carbon or heteroatom. Due to the nature of this connectivity spiranes are non-planar which is underlined by their name "spirane", derived from the Latin word *spira*, meaning twist or whorl.



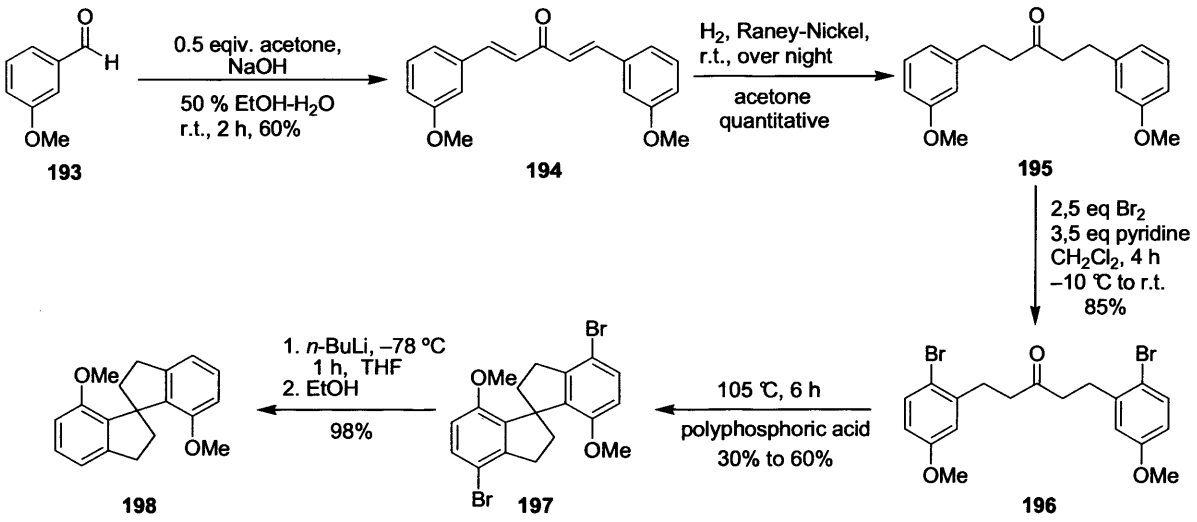
Scheme 5.19: *Types of chiral spiranes*

The connecting atom of the two rings is called spiroatom and shows axial chirality; especially a quaternary carbon in this position is configurationally stable and racemisation impossible. Changes in the conformation can only be attained by the distortion of the whole molecule. This feature is different to the biaryl-systems already mentioned in Chapter 5.4.1, which depend on the restricted rotation about the central bond and therefore on the bulk especially of the *ortho*-substituents. As shown in Scheme 5.19, chiral spiranes consisting of two same-sized ring systems can be discerned into three types: "**A**, which definitely displays axial chirality similar to that of allenes and alkylidenecycloalkanes; **B**, which, like corresponding alkylidenecycloalkanes displays central rather

then axial chirality; and **C**, which conceptually would appear to display axial chirality but, for purposes of nomenclature, is considered to have a chiral centre (Cahn, Ingold, and Prelog, 1966)."[119]

The spirane scaffold discussed within this thesis belongs into the group of type **C**. In order to establish the absolute configuration of molecules in this class, one ring is chosen randomly over the other and the more substituted branch in this ring system has priority one, whereas the less substituted has priority three. In the less favoured ring the more branched atom has priority two and the less branched four. The spirocentre is considered as a chiral centre. In accordance with these rules, compound **C** is named (*R*)-1,1,5,5-tetramethyl-spiro[3,3]heptane.

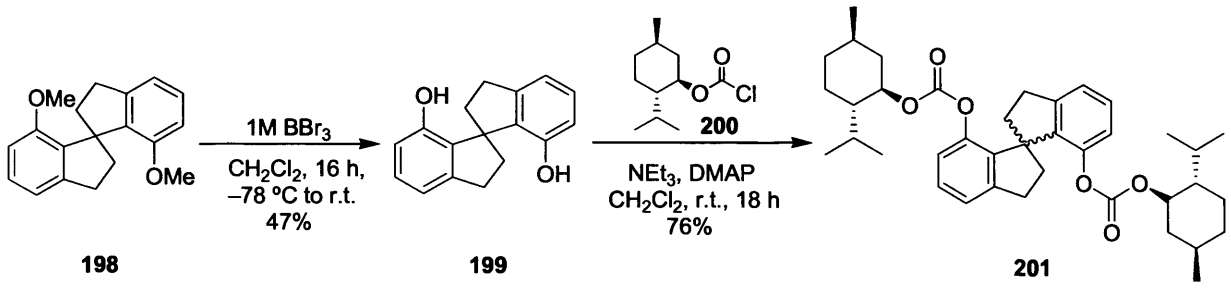
Birman and co-workers established a relatively easy synthetic route to spirobiindanes[120] which also allows limited substitution at some of the positions on the indane scaffolds. The synthesis of the racemic SPINOL (**199**), the separation of the two isomers, and the conversion into the hydrogen phosphate (analogue to the procedure for the BINOL-phosphoric acids) is presented in the next paragraphs.



Scheme 5.20: *Synthesis of the spirobiindane scaffold*

Commercially available 3-methoxy benzaldehyde **193** is used as starting material for the synthesis of the methyl-protected spirobiindane **198** (Scheme 5.20). A double Aldol reaction of *m*-anisaldehyde and acetone in the presence of aqueous sodium hydroxide afforded ketone **194** in 60% yield after column chromatography. Subsequent hydrogenation over Raney-Nickel (24 h) in acetone afforded pure **195**, which was brominated without further purification. The bromination is necessary to ensure that the following cyclisation is only occurring in the 2-position of the aromatic system. Dibromide **196** was obtained in 85% yield after purification over silica gel chromatography. The following cyclisation of **196** with polyphosphoric acid at 105 °C led to poor to reasonable yields (30-60%) of spirobiindane **197**. At this stage of the synthesis it is generally possible to either cleave the bromine

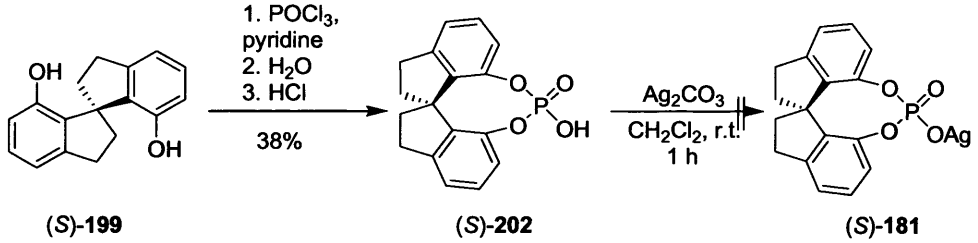
from the aromatic ring or use the functionality for additional substitution reactions. For initial investigations of the phosphoric acid's ability to induce chirality, the unsubstitued scaffold was preferable. Hence, **197** was subjected to *n*-BuLi in THF followed by ethanol to afford **198** in 98% yield. Then, demethylation with boron tribromide in dichloromethane led to racemic SPINOL (1,1'-spirobiindande-7,7'-diol) **199** (Scheme 5.21). An efficient resolution of the diol mixture was achieved by esterification with *L*-menthyl chloroformate **200**.[118] The corresponding diastereomers **201a/201b** were easily separated by column chromatography.



Scheme 5.21:** Synthesis and separation of the enantiomers of SPINOL **199

One isomer was obtained as oil which corresponds to the menthyl ester of (*R*)-SPINOL **201a**, whereas the ester of (*S*)-SPINOL **201b** occurred as a solid at ambient temperature. The menthyl formate esters **201a/201b** were cleaved separately with potassium hydroxide in a mixture of water and ethanol 1:1 with good yields.[121]

(*S*)-Diol **199** was then converted into phosphoric acid (*S*)-**202** analogue to the procedure used for the synthesis of the BINOL-phosphoric acids. Treatment of (*S*)-**199** with phosphorous oxychloride in pyridine afforded (*S*)-**202** [SPINOL-P; (*S*)-1,1'-spirobiindande-7,7'-diylhydrogenphosphate] in 38% yield.



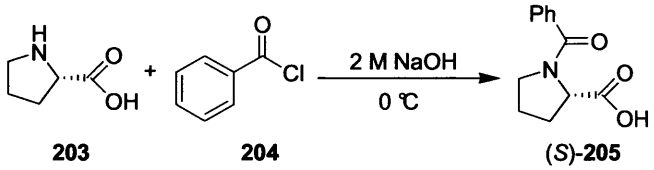
***Scheme 5.22:** Attempted synthesis of (S)-AgSPINOL*

It was planned to convert (*S*)-**202**, similar to the BINOL derivates, into the silver salt using silver carbonate in dichloromethane. The workup for **153** (TRIP) involved the filtration through celite, therefore the organic solution of the reaction mixture was subjected to the same workup procedure. Unfortunately, neither the phosphoric acid nor the silver salt could be isolated after filtration, which

suggested the adherence of the product and/or starting material on the Celite plug. Further H^+/Ag^+ exchange reactions were not attempted. However, it was anticipated that the selenenylation reaction could also occur using the phosphoric acid directly, given the right reaction conditions. This presumption is further detailed in Chapter 5.5.

5.4.3 Carboxylates and Sulfonates

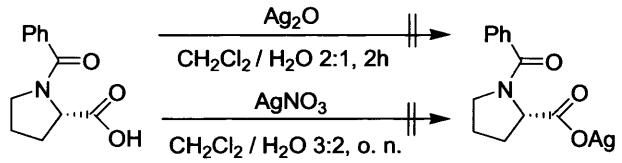
The synthesis of phosphoric acids was, although straightforward, quite time consuming. To synthesise smaller and more easily accessible chiral counteranions was therefore desirable. Chiral amino acids like *L*-proline **203** have proven to be promising organocatalysts on different occasions. Enantiomerically pure *L*-proline is commercially available and cheap.



203 **204** (*S*)-**205**

Scheme 5.23: *Synthesis of chiral carboxylic acid using proline*

To overcome the solubility problem of the amino acid in organic and less polar solvents (desirable due to the need of close ion pairing during the selenenylation reactions) **203** was benzoylated.[122] It was then attempted to convert the carboxylic acid functionality into the silver salt.

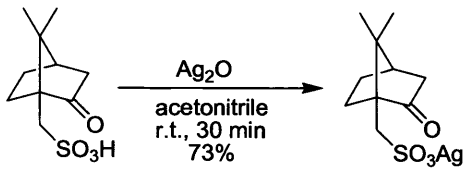


(*S*)-**205** (*S*)-**183**

Scheme 5.24: *Attempted conversion of (S)-205 into silver salt (S)-183*

Unfortunately, neither silver(I) oxide, nor silver nitrate led to the desired product. Additionally, the reisolation of compound (*S*)-**205** from the aqueous media was challenging and led only to low yields.

Another commercially available reagent that could be potentially used as a chiral counteranion is (*S*)-(+)-camphorsulfonic acid **206**. In this case, the synthesis of silver salt **182**, employing silver oxide, occurs within 30 min in acetonitrile in 73% yield from the readily available camphorsulfonic acid (Scheme 5.25).[123]

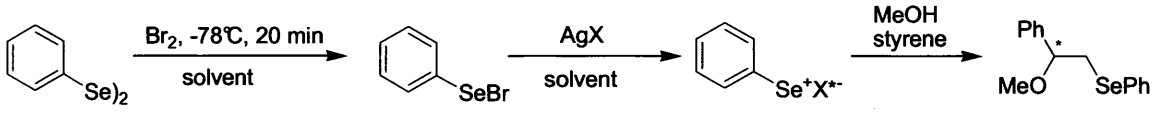


206 **(*S*)-182**

Scheme 5.25: *Synthesis of silver camphorsulfonate (S)-182*

5.5 Reactions with Chiral Counteranions

Ideally, the use of an unsubstituted selenenyl halide like phenylselenenyl bromide together with a chiral counteranion would form a new chiral selenenylating reagent to achieve a stereoselective reaction pathway during a selenenylation reaction.



207 **208** **209** **210**

Scheme 5.26: *General reaction using chiral counteranions to generate new chiral selenenylating reagents*

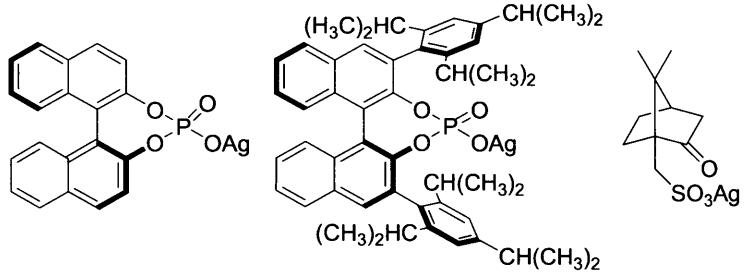
To test this hypothesis, phenylselenenyl bromide **208** was generated from diselenide **207**, and the synthesised silver salts (Chapter 5.4) were added neat or in methanolic solution. In principle this approach would lead to the formation of the envisioned chiral reagents and hence to enantiomeric enriched products when reacting with styrene (Scheme 5.26).

5.5.1 Reactions with Phenylselenenyl Bromide

Initially, phenylselenenyl bromide **208** was used together with (*S*)-**179**, the silver salt of (*S*)-BINOL-P. Three different solvents with regards to their polarity were chosen: diethyl ether, dichloromethane and toluene. It was expected that the selectivity, if any could be observed would increase from the more to the less polar solvents.

Unfortunately, (*S*)-**179** proved to be barely soluble at room temperature in dry diethyl ether and small amounts of dry methanol, which is used as the standard nucleophile during these reactions. Despite these findings, the silver salt was added neat to a solution of the selenenyl bromide **208** in diethyl ether at –78 °C. However, no reaction occurred in diethyl ether at –78 °C. After warming the mixture to

0 °C and stirring overnight, a small amount of product **210** was formed. After a short filtration through silica gel, the reaction mixture was investigated with high pressure liquid chromatography (HPLC) using a chiral column to determine if any diastereomeric excess could be observed. This was not the case. In general there are two primary possibilities for the failure of this first reaction: A flaw in the concept and the solubility of silver salt (*S*)-**179**.



(*S*)-**179** (*S*)-**180** (*S*)-**182**

Scheme 5.27: *Chiral acids as counteranions for achiral electrophilic selenium*

Table 5.4 *Methoxyselenenylation reaction with phenylselenenyl bromide, styrene and different silver salts*

Silver salt	Solvent	Yield [%]	*e.e.* [%]
(*S*)-**179**	diethylether	21	0
(*S*)-**179**	dichloromethane	53	3
(*S*)-**179**	toluene	-	-
(*S*)-**180**	diethylether	10	0
(*S*)-**180**	dichloromethane	48	1
(*S*)-**180**	toluene	24	1
(*S*)-**182**	acetonitrile	18	0

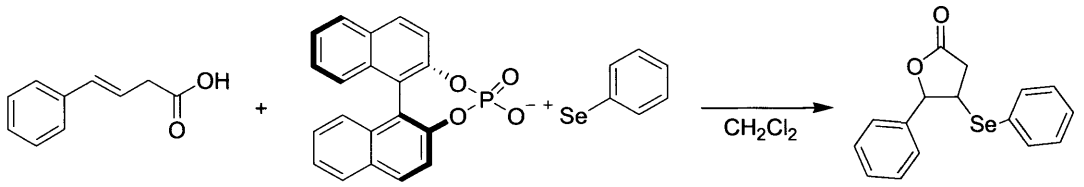
The solubility problem of the silver salt improved when the reaction was carried out in dichloromethane. After addition of methanol and styrene, the reaction was stirred for 2 h at –78 °C, then warmed to 0 °C and stirred for additional 3 h. Product **210** was formed in 53% yield and HPLC analysis confirmed 3% diastereomeric excess. Although this result is within the tolerable defect parameter of the HPLC system, the result encouraged a further test using toluene as the solvent to prevent a possible unfavourable dissociation of the ion pair. However, even at 0 °C no reaction occurred, assumedly again because of solubility reasons. Table 5.4 gives an overview of the results.

With further investigations using different silver salts, it should be established if the encountered low enantiomeric excesses were due to a general problem in the course of these reactions or if the properties of the chosen silver salt (*S*)-**179** were insufficient to positively influence the methoxyselenenylation. Compound (*S*)-**180** was used under identical reaction conditions as mentioned above. It was possible to obtain 1% *e.e.* using dichloromethane and toluene as solvents. However, this

was again within the tolerable defect parameter of the HPLC system. In diethyl ether, the product was again racemic.

As the BINOL-derived anions were not able to enhance the enantiomeric excess, the silver salt of camphorsulfonic acid (*S*)-**182** was employed. Due to the polarity of (*S*)-**182**, the methoxyselenenylation reaction had to be carried out in acetonitrile at –40 °C under otherwise identical reaction conditions. In this case the product also was racemic.

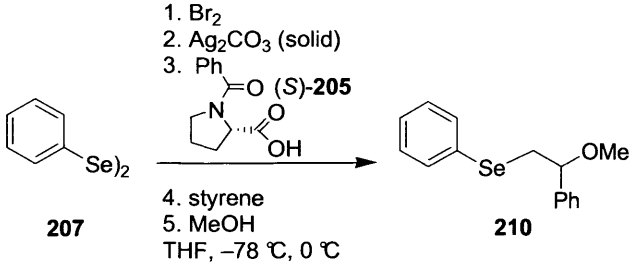
To exclude the possibility that the use of styrene or methanol were major influences, (*S*)-**179** was tested in a cyclisation reaction with acid **211** (Scheme 5.28).



211 **209a** **212**

Scheme 5.28: *Selenocyclisation reaction with phenylselenenyl-BINOL-P [(S)-**209a**]*

The selenenyl salt **209a** was assumed to be obtained from diphenyl diselenide **207** by reaction with bromine and (*S*)-**179** in dichloromethane at –78 °C. The selenocyclisation was carried out at room temperature by addition of (*E*)-4-phenylbut-3-enoic acid **211**. The product **212** was obtained in 26% yield after 4 hours stirring. According to HPLC measurements the chiral counteranion again did not show any influence in the stereochemical outcome of the reaction, the product was obtained as a racemate.



207 **210**

Scheme 5.29: *Methoxyselenenylation with (S)-**205** as chiral source*

As it was not possible to obtain silver salt (*S*)-**183**, a different approach was used to investigate its ability to influence the stereochemical outcome of these reactions. The chiral anion was generated *in situ* when the phenylselenyl bromide **208** was treated with silver(I) carbonate which led to the

precipitation of silver bromide. The carbonate counteranion should be easily exchanged by *N*-benzoylproline (*S*)-**205** due to the higher acidity of the carboxylic acid (Scheme 5.29).

Table 5.5: *Methoxyselenenylation with (S)-**205** as chiral source*

Solvent	Temperature [°C]	Yield [%]	*e.e.* [%]
tetrahydrofuran	–78	50%	0
toluene	–78	n.d. [b]	0
CPME[a]	–78	n.d. [b]	3
toluene/CPME 19:1	–78	n.d. [b]	2
chlorobenzene	0	n.d. [b]	0

[a] CPME: cyclopentylmethyl ether , [b] n. d.: not determined

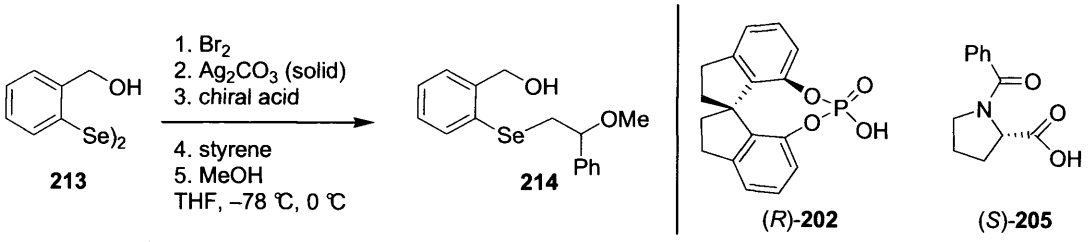
In Table 5.5 the results of the methoxyselenenylation reaction in different solvents are summarised. The obtained enantiomeric excesses in all reactions were still 3% or below.

The described experiments indicated that the successful manipulation of selenenylation reactions using unfunctionalised selenenyl halides as starting materials is improbable.

5.5.2 Reactions with Functionalised Selenenyl Bromides

In the published literature, where the nature of the counteranion seems to have a considerable influence on the selectivity and the yield of the reactions, the employed selenium electrophiles have a common characteristic, a close proximity of a heteroatom to the selenium atom.

Therefore achiral diselenide **213** was employed as precursor for the generation of chiral selenenylating reagents using chiral acids as counteranions. The reagents have a heteroatom in close proximity to the electrophilic selenium atom which could also act as an "anchor" for the chiral anion.



Scheme 5.30: *Methoxyselenenylation reaction with diselenide **213** and styrene*

N-Benzoyl-*L*-proline [(*S*)-**205**] and (*R*)-SPINOL-P [(*R*)-**202**] were employed together with tetrahydrofuran and toluene as medium for these reactions (Table 5.6). It was assumed that if chiral counteranions would have any influence on the course of these reactions, the two chosen acids (*S*)-**205**

and (*R*)-**202** and a small range of solvents should be sufficient to show at least a small degree of stereoinduction (≥ 5% *e.e.*). Only the use of tetrahydrofuran led to the formation of some product which was in all three cases essentially racemic. The reason for the failure of the reactions using toluene was not further analysed, but could be due to the use of silver carbonate which likely failed to dissolve in the unpolar solvent. This would lead to the addition of selenenyl bromide onto the styrene double bond which could be reversed during basic aqueous workup.

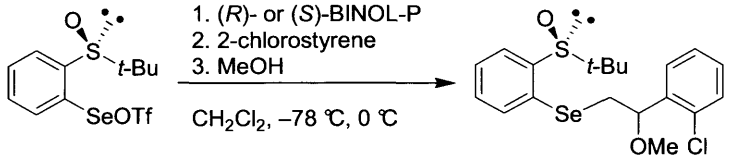
Table 5.6: *Methoxyselenenylation reaction with diselenide **213** and styrene*

Acid	Solvent	Conversion [%][a]	*e.e.* [%]
(*S*)-**205**	tetrahydrofuran	29	2
(*S*)-**205**	tetrahydrofuran /toluene 1:1	21	0
(*S*)-**205**	toluene	-	-
(*S*)-**202**	tetrahydrofurane	31	0
(*S*)-**202**	toluene	-	-

[a] Determined after workup with crude NMR spectra.

As the obtained results were still rather discouraging, no further attempts were made using other solvents or chiral organic acids.

Instead it was investigated if an already chiral selenenylating reagent, which was showing good selectivities, could be enhanced by the addition of chiral acids (Scheme 5.31). Therefore chiral diselenide (*S*)-**54** was employed with (*R*)-**179** using the same reaction conditions established for the methoxyselenenylation of 2-chlorostyrene in dichloromethane (*d.r.*: 11:1) in Chapter 3.3.



(*S*)-**99** **101**

Scheme 5.31: *Methoxyselenenylation reaction with selenenyl triflate (S)-**99** and 2-chlorostyrene*

In the course of this experiment, (*R*)-**179** did not easily dissolve in dichloromethane at –78 °C. As it was anticipated that only the dissolved phosphoric acid would be able to form a chiral reagent in sufficient quantity, 0.5 ml of dry methanol were added before the addition of 2-chlorostyrene. Product **101** was obtained in 35% yield and the diastereomeric ratio was determined as 6:1 according to the crude NMR.

This result seemed to be promising as the drop in selectivity could be due to the mismatched pair of stereocentres of selenium electrophile (*S*)-**99** and phosphoric acid (*R*)-**179**. Therefore the reaction was

repeated with a matched pair of (*S*)-**99** and the (*S*)-**179** under otherwise identical reaction conditions. However, this led again to a drop in the diastereomeric ratio to 5.5:1.

The reason for these results can be assumed to be the change in reaction conditions. The addition of methanol before the addition of styrene changed the overall polarity of the solvent considerably and hence made it more polar. One obvious result during the previous studies (Chapter 3.3) was that an increase of solvent polarity led to a decrease in selectivity.

Further investigations into the use of chiral anions for the production of chiral selenenylating reagents were dropped at this point as they did not seem very promising.

6. New Diselenides as GPx Mimics

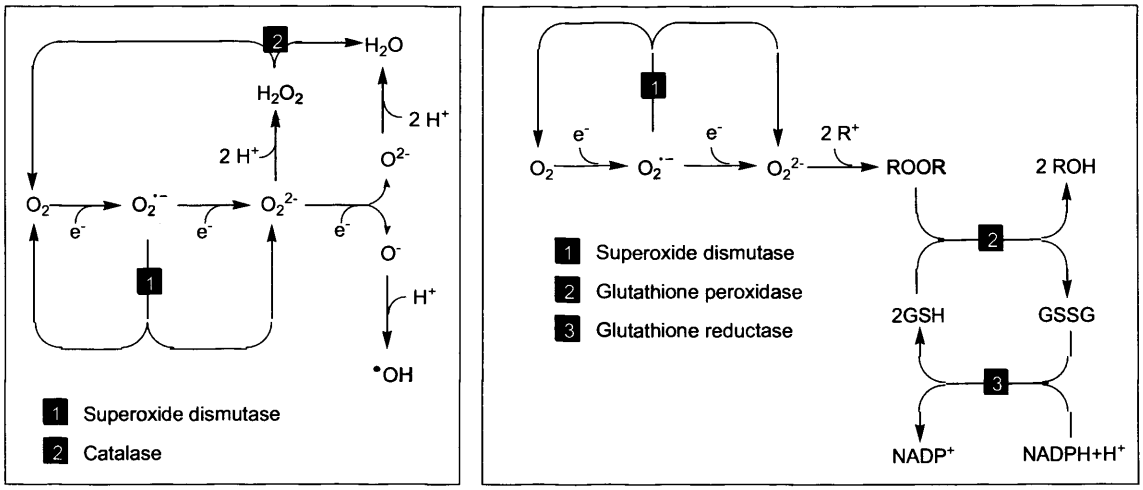
6.1 Introduction

Some of the diselenides synthesised in the course of this thesis were tested as mimics for the family of glutathione peroxidases (GPx) – a class of antioxidant selenoenzymes – in the group of Professor G. Mugesh in Bangalore, India. All presented experiments were carried out by Debasish Bhowmick, a current PhD student in the research group of Prof. Mugesh. It was possible however, during a five week stay in Bangalore, to observe and test the two employed experimental procedures and examine the observed results. The background for the presented investigations and the preliminary results are highlighted in this chapter.

6.1.1 Oxidative Stress and Glutathione Peroxidases (GPx)

All living aerobic cells are depending on molecular oxygen for the production of energy. This dependence however also has some negative aspects. The metabolism of O_2 constantly generates a small amount of reactive oxygen species (ROS) which are free radicals or strong oxidants: superoxide radicals ($\cdot O_2^-$), peroxide anions (O_2^{2-}) which react with two protons to hydrogen peroxide (H_2O_2), and oxygen anions (O^-) which after protonation generate hydroxyl radicals ($\cdot OH$). All of these species are able to damage cellular structures and other highly functionalised molecules within the cell (Scheme 6.1).[124] The formation of ROS is catalysed by metal ions, e.g. iron, in the catalytic centre of enzymes, or co-enzymes, like FMN (flavin-mononucleotide) and FAD (flavin-adenin-dinucleotide).

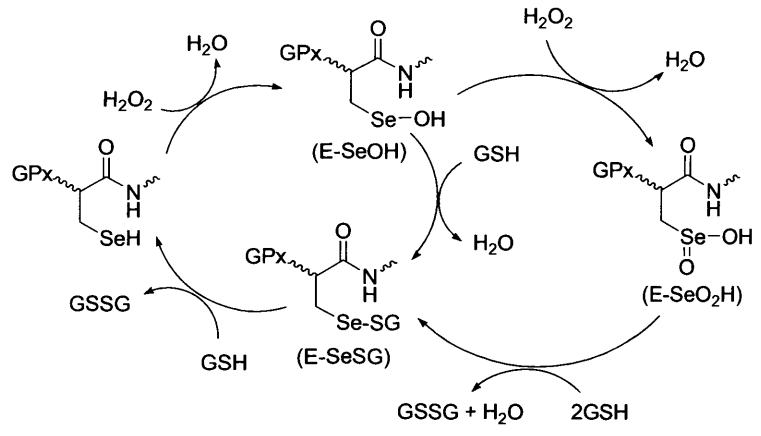
Beside molecules which can act as antioxidants, like α-tocopherol, ubiquinol, ascorbic acid, β-carotine, bilirubin and glutathione, there are several enzymes able to render the ROS harmless. One major enzyme class in the defence against ROS are the superoxide dismutases (SOD), which catalyse the dismutation of superoxide radicals into oxygen and hydrogen peroxide. The latter can be disposed by another enzyme called catalase which generates water and oxygen (Figure 6.1).[122]



Scheme 6.1: *Biological pathways leading to ROS and respective defence mechanisms.*

Another class of antioxidant enzymes are glutathione peroxidases (GPx). These selenoenzymes catalyse the reduction of harmful peroxides at the expense of gluthatione (GSH) to protect various organisms from oxidative stress.[125] The reactive species at the active site of these enzymes of the GPx superfamily is a selenol moiety. The four known GPx enzymes are the classical cytosilic GPx (cGPx), phospholipid hydroperoxide GPx (PHGPx), plasma GPx (pGPX) and the gastrointestinal GPx (giGPX).[126]

As detailed in Scheme 6.2, the selenol moiety (R-SeH) in the active site of these enzymes is oxidised by hydrogen peroxide to the corresponding selenenic acid (R-SeOH). This species is then reduced by glutathione (GSH) to the selenenyl sulfide intermediate (R-SeSG). A second molecule of GSH then attacks the mixed species and regenerates the active form of the enzyme. Two equivalents of GSH are oxidised to the corresponding disulfide, while hydroperoxide is reduced to water or alcohol. If the concentration of peroxides is higher, the selenenic acid can be oxidised further to the corresponding seleninic or selenonic acids. Both species can also be reduced by GSH to the selenenyl sulfide.



Scheme 6.2: *Proposed catalytic cycle of GPx*

The excellent anti-inflammatory, anti-atherosclerotic and cytoprotective properties of Ebselen as GPx mimetic attracted much research around the design and synthesis of new GPx mimetics. The determination of GPx-like antioxidant activity of organoselenium compounds can be measured by several methods such as NMR spectroscopy,[127] UV-visible spectroscopic methods,[128] enzymatic methods[129] and by HPLC assays[130]. In this research two different assays are used, an HPLC-based assay employing thiophenol and an UV-visible spectroscopic method utilising the UV absorption of NADPH. Both methods are detailed in Chapters 6.2 and 6.3.

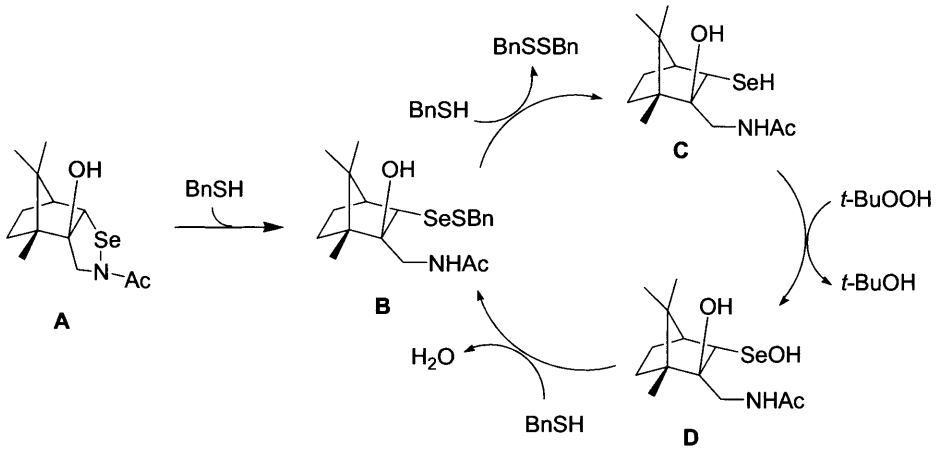
It has been observed that GPx follows the typical Michaelis-Menten kinetics. The rate for the reduction of peroxide gets saturated at a very high concentration of the peroxide substrate and thiol co-substrate.[131] At a very high concentration of the substrate, the enzyme-substrate complex is expected to be the predominant species and thus the concentration of the free enzyme to catalyse a new substrate becomes negligible. This generally leads to the saturation kinetic pattern. Furthermore, the efficiency of different enzymes can be quantitatively determined by using a Lineweaver-Burk plot in which the reciprocal of the reaction rate is plotted against the reciprocal of the substrate concentration. The kinetic parameters such as maximum velocity (V_{max}), the Michaelis constant (K_M), the catalytic constant or turnover number (k_{cat}), and the catalytic efficiency (η) can be determined using these double-reciprocal plots. The catalytic efficiency ($\eta = k_{cat}/K_M$) is used to understand the relative activities of enzymes and their mimics to catalyse different substrates. So called "perfect enzymes" show turnover numbers between 10^8 to 10^9 $M^{-1}s^{-1}$, which means that the reaction is only limited by the substrate diffusion rate. Singh *et al.* have shown that some of the GPx mimics also exhibit enzyme-like kinetic behaviour,[126c] however this can also deviate from saturation upon increasing the thiol concentration depending on the strength of selenium-heteroatom non-bonded interactions.

6.2 HPLC Based Thiophenol Assay

6.2.1 Background

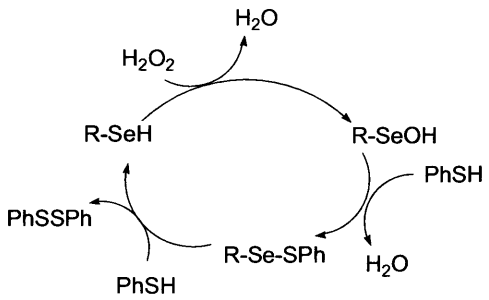
In order to measure the ability of a selenium compound to act as a glutathione peroxidase mimic, Back and Dyck developed an HPLC assay during which the activity of the selenium compound can be determined.[128] In natural systems, disulfide (GSSG) is formed from glutathione (GSH). The latter can be substituted by a UV-active thiol such as phenylmethanethiol (BnSH). The formation of dibenzyldisulfide (BnSSBn) could occur if a glutathione peroxidase mimetic is used together with an oxidant. Employing HPLC methods, the amount of disulfide formed could be monitored. Plotting the percentage formation of a disulfide against reaction time would then give a measurement for the ability of a selenium compound to act as a glutathione peroxidase mimetic.

Using this strategy, Back and Dyck found that dibenzyldisulfide is generated during a catalytic cycle from phenylmethanethiol (BnSH) via the oxidation by a selenenamide procatalyst **A** (Scheme 6.3). The resulting selenenylsulfide **B** undergoes further attack by the thiol to generate dibenzyl disulfide and selenol **C**. *t*-Butyl hydroperoxide (*t*-BuOOH) then oxidises **C** to the seleninic acid **D**, which reacts with another equivalent of thiol to regenerate the true catalyst, selenenylsulfide **B**. Naphthalene was employed as an internal standard in this process. For a typical procedure, a solution of phenylmethanethiol and naphthalene in dichloromethane is treated with *t*-BuOOH. Upon addition of the selenium procatalyst, the reaction progress is monitored by a reverse phase HPLC method over time.



Scheme 6.3: *Catalytic cycle during Back's HPLC assay*

Back's procedure was modified by Mugesh and co-workers using a mixture containing a 1:2 molar ratio of thiophenol (PhSH) and a peroxide in methanol at room temperature as model system. A typical procedure includes the periodical injection of aliquots into a reversed phase column (Lichrosphere 60, RP-select B, 5μm) using methanol and water (95:5) as eluent.



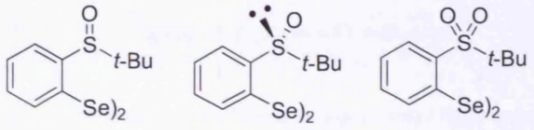
Scheme 6.4: *Catalytic cycle in HPLC Assay used by Mugesh*

The concentrations of diphenyl disulfilde (PhSSPh) are determined at a wavelength of 254 nm using pure PhSSPh as an external standard. The amount of disulfide formed during the course of these reactions was calculated from the calibration plot for the standard (PhSSPh). Runs with and without

catalyst were carried out under the same conditions. The catalytic cycle, using a potential GPx mimetic, is shown in Scheme 6.4.

6.2.2 Results

The catalytic activities of three diselenides – *rac*-**54**, (*S*)-**54** and **87** – (Scheme 6.5) were tested and compared using the thiophenol-based HPLC assay developed by Mugesh and co-workers.



rac-**54** (*S*)-**54** **87**

Scheme 6.5: *Tested selenium compounds*

Identical experimental conditions were employed during the assays using three different peroxides (hydrogen peroxide, *t*-butyl hydroperoxide and cumene hydroperoxide). The formation of diphenyl disulfide (PhSSPh) was monitored by reversed-phase HPLC at 254 nm. The conversion (%) was calculated from previously established calibration plots and plotted against the time (min) (Figure 6.1). The standard assay conditions use 10.0 μM solutions of catalysts in *N*,*N*-dimethylformamide, 1.0 mM solutions of PhSH and 2.0 mM solutions of peroxides in MeOH at 23 °C. The control reactions were performed under identical assay conditions in the absence of diselenides.

Figures 6.1 to 6.3 show that the selenium catalysts follow indeed typical saturation kinetics. Using these plots, the t_{50} values – a measurement for the activity of the different diselenide catalysts – were obtained. They are shown in Table 6.1.

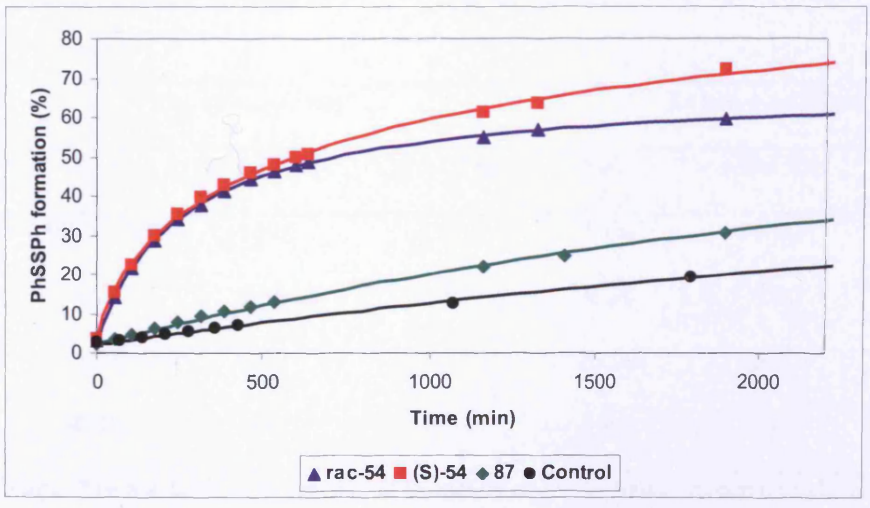


Figure 6.1: *Diphenyl disulfide (PhSSPh) formation (%) plotted against time using hydrogen peroxide.*

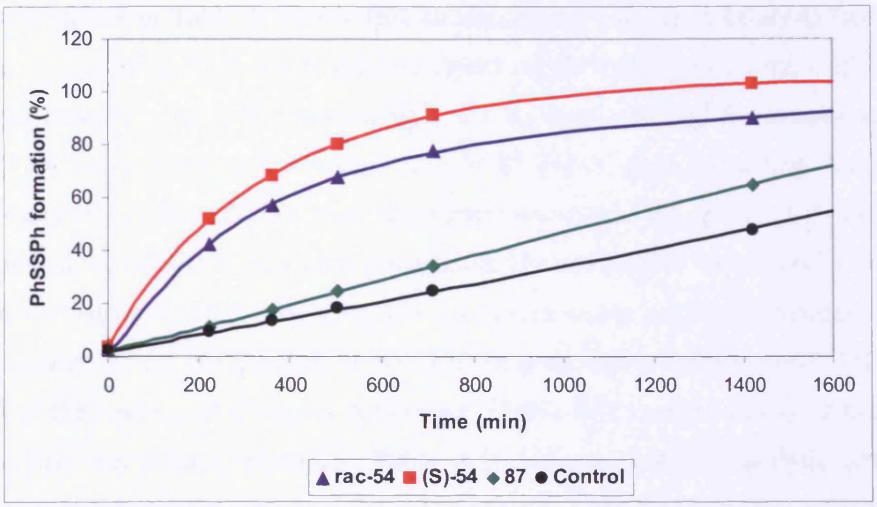


Figure 6.2: *PhSSPh formation (%) plotted against time using t-butyl hydroperoxide.*

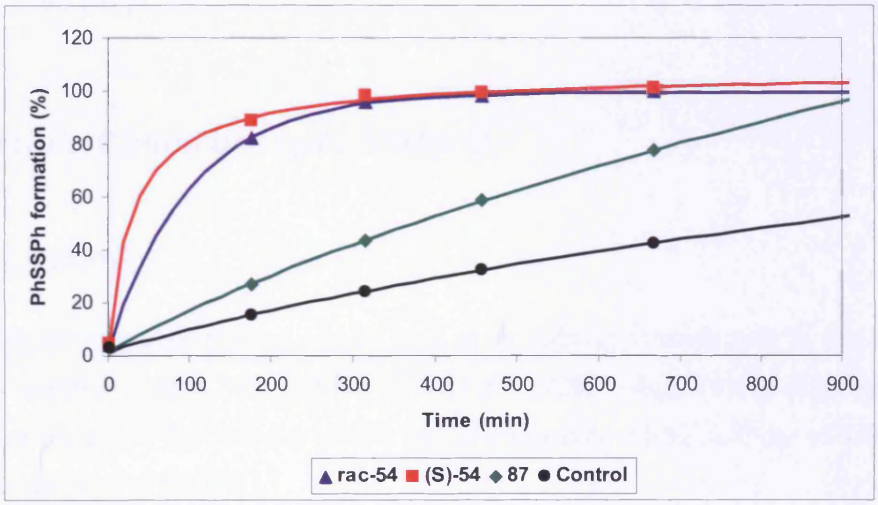


Figure 6.3: *PhSSPh formation (%) plotted against time using cumene hydroperoxide.*

Table 6.1: *t_{50}-values for the reduction of peroxides by PhSH in the presence of diselenides rac-**54**, (S)-**86** and **87** at 23 °C.*

Compound	t_{50} values (min)[a]			Relative activities[b]		
	H_2O_2	*t*-BuOOH	Cum-OOH	H_2O_2	*t*-BuOOH	Cum-OOH
Control[c]	44% > 6000	1498	838	1.00	1.00	1.00
rac-**54**	641	294	73	9.36	5.10	11.48
(*S*)-**54**	550	220	55	10.90	6.80	15.23
87	4218	1062	371	1.42	1.41	2.26

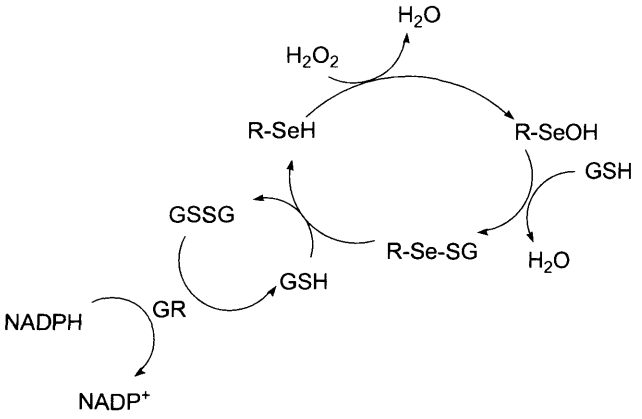
[a] Assay conditions: The reactions were carried out in MeOH at 23 °C. Selenium compounds: 10.0 μM; PhSH: 1.0 mM; peroxide: 2.0 mM. [b] Relative activities are given with respect to the corresponding control values. [c] Control: Assay conditions are identical to [a] without selenium catalyst.

The results summarised in Table 6.1 show that all diselenides can act as catalysts, compared to the control values. However, the sulfoxide-based diselenides *rac*-**54** and (*S*)-**54** are more efficient catalysts than the sulfone-based diselenide **87**. For example, the t_{50} value obtained for compound *rac*-**54** (641 min) in the H_2O_2 assay is much lower than that of **87** (4218 min), indicating that the sulfoxide substituted compound *rac*-**54** is almost seven times more active than the sulfone derivative **87**. Despite the observation that the sulfoxide-based compounds (*rac*-**54** and (*S*)-**54**) were found to be much better catalysts than derivative **87**, the relatively low t_{50} values using organic peroxides (*t*-BuOOH or Cum-OOH) compared to the H_2O_2 assay can be ascribed to the facile oxidation of PhSH by *t*-BuOOH or Cum-OOH in the absence of selenium compounds (Table 6.1, Control values). Nevertheless, it is also observed that the relative activities (Table 6.1) indicate that the catalytic activities of all diselenides strongly depend on the nature of the peroxide. This is interesting, as Mugesh and co-workers have shown that the nature of peroxide has very little effect on the GPx-like activity of Ebselen and related compounds.[132]

6.3 UV-visible Spectroscopic Method

6.3.1 Background

The UV-visible spectroscopic method can be used as an indirect measurement of the activity of the native GPx enzymes as well as their mimics.[133] The GSH-GSSG coupled assay employed by Mugesh and co-workers shown in Scheme 6.6 allows the determination of the activity of GPx mimics by monitoring the decrease of NADPH.



Scheme 6.6: *GSH-GSSG coupled assay (GR: glutathione reductase)*

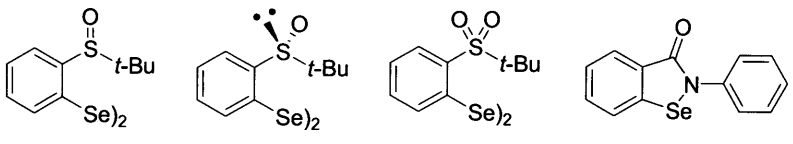
A selenium catalyst, in the presence of H_2O_2 as substrate, is oxidised to the corresponding seleninic acid which is reduced by GSH to the corresponding selenenyl sulfide. Another equivalent GSH releases the selenol and produces GSSG. The naturally occurring enzyme glutathione reductase (GR)

reduces the disulfide to the oxidised GSH. The reductase however depends on NADPH as a co-factor. The oxidation of NADPH to $NADP^+$ to recycle the glutathione reductase leads to a steady increase in $NADP^+$. Employing a UV-visible spectroscopic method, it is possible to follow a decrease in the absorbance at 340 nm, the absorbance maximum of NADPH. Hence this observation provides an indirect spectrophotometric tool for monitoring GPx-like antioxidant activity. The decrease in the absorbance at 340 nm is directly proportional to the GPx activity of the test compound. The assay mixture is generally prepared by dissolving EDTA, glutathione (GSH), NADPH, glutathione reductase (GR) and an appropriate amount of the test compound in potassium phosphate buffer. The reaction is initiated by the addition of H_2O_2, and the decrease in absorbance at 340 nm (A340) is recorded with time.

Ebselen **215** (Scheme 6.7), a lipid-soluble organoselenium compound, was already mentioned as a well-known GPx mimic. It is a potent scavenger of hydrogen peroxide and other ROS.[134] Currently, Ebselen undergoes clinical trials and indeed exhibits antioxidant and other biological activities both in *in vitro* and *in vivo* systems.[135] Additionally, it shows antitumor and immuno-modulating activities and has been suggested to have a potential to protect ROS-mediated brain damage.[136] Due to the good results obtained as a GPx mimic it is used as a standard in the UV-visible spectroscopic measurements.

6.3.2 Results

The GPx activity was monitored spectrophotometrically by following the procedure established by the group of Prof. G. Mugesh, IISc, Bangalore. The test mixture contained GSH (2.0 mM), EDTA (1.0 mM), glutathione disulfide reductase (1.0 unit/ml) and NADPH (0.4 mM) in 0.1 M potassium phosphate buffer of pH 7.5. The test compounds (80 μM) were added to the assay mixture at room temperature and the reaction was started by the addition of peroxide (1.6 mM). The initial reduction rates were calculated from the rate of NADPH oxidation at 340 nm in the GSH assay. Each initial rate was measured at least three times and calculated from the first 5-10% of the reaction by using $\xi_{mM} = 6.22\ mM^{-1}cm^{-1}$ as the millimolar extinction coefficient for NADPH at 340 nm and a 1 cm light path. For the peroxidase activity, the rates were corrected for the background reaction between peroxide and thiol.



rac-**54** (*S*)-**54** **87** **215**

Scheme 6.7: *Tested selenium compounds*

Table 6.2: *Initial rates (v_0) for the reduction of hydrogen peroxide by glutathione (2 mM) in the presence of different catalysts (80 μM) at 25 °C.*

Compound	Initial rates, v_0 ($\mu Mmin^{-1}$)
rac-**54**	99.1
(*S*)-**54**	76.6
87	21.3
Ebselen	35.1

Assay condition: Phosphate buffer (100 mM), glutathione reduced (2 mM), NADPH (0.4 mM), EDTA (1 mM), glutathione reductase (1 unit), peroxide (1.6 mM), and test compound (80 μM).

The catalytic activity of different catalysts can be compared when the initial rate with various concentrations of glutathione is observed. The plots showing the initial rates against the concentration of GSH were obtained using a fixed concentration of 1.6 mM hydrogen peroxide (Figure 6.4).

As already observed during the HPLC-based assay, diselenides *rac*-**54**, (*S*)-**54** and **87** as well as Ebselen are displaying typical saturation kinetics, which are generally observed for enzymatic reactions (Figure 6.4).[129] These saturation kinetics can be used to determine the catalytic parameters for the selenium catalysts *rac*-**54**, (*S*)-**54** and **87** as well as for Ebselen. The most widely used diagrams for this purpose are Lineweaver-Burk double-reciprocal plots, where the reciprocal of initial rates ($1/v_0$) is plotted against the reciprocal of the substrate concentrations (1/[substrate]), which leads to linear lines (Figure 6.5).

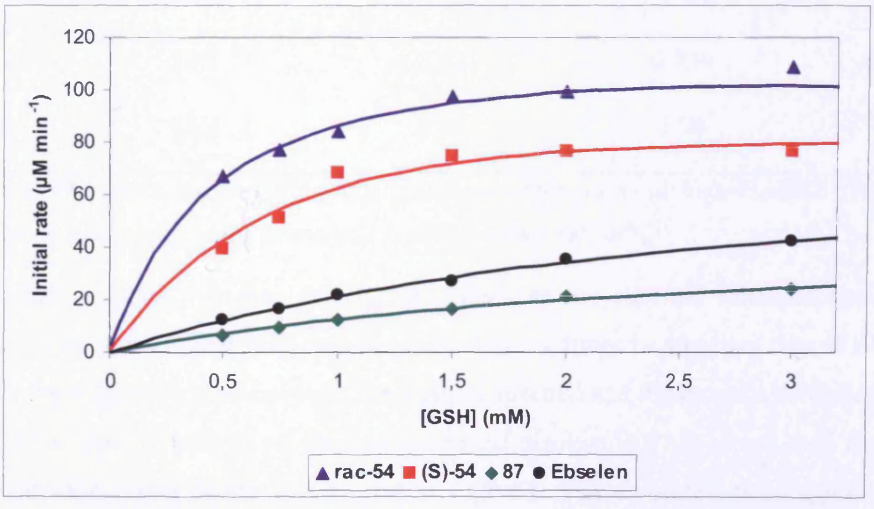


Figure 6.4: *The initial rate is plotted against the concentration of GSH, using a fixed concentration of 1.6 mM hydrogen peroxide*

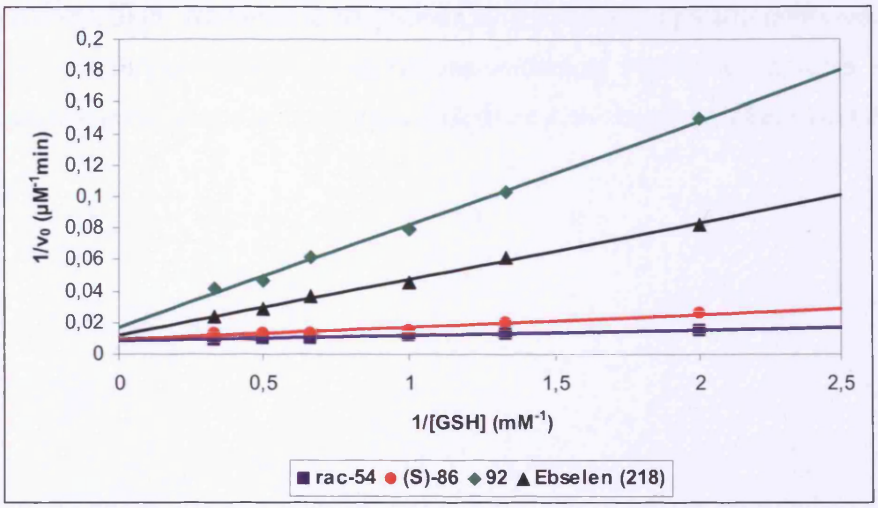


Figure 6.5: *Lineweaver-Burk plot obtained for different catalysts at various concentrations of GSH with 1.6 mM hydrogen peroxide and 80µM selenium catalyst.*

Using the Lineweaver-Burk double-reciprocal plot, the maximum velocity (V_{max}), the Michaelis constant (K_M), the catalytic constant or turnover number (k_{cat}), and the catalytic efficiency (η) were obtained.

Table 6.3: *Effect of thiol concentrations on the maximum velocity (V_{max}), Michaelis constant (K_m), catalytic constant (K_{cat}), and catalytic efficiency (η) for compound rac-**54**, (S)-**54**, **87** and Ebselen at a fixed concentration of 1.6 mM H_2O_2.*

Catalyst	V_{max} ($\mu M min^{-1}$)	K_m (mM)	K_{cat} (min^{-1})	η ($M^{-1}min^{-1}$)
rac-**54**	121.9	0.417	1.52	3.64×10^3
(S)-**54**	110.6	0.868	1.38	1.58×10^3
87	58.7	3.83	0.734	1.91×10^2
Ebselen	85.3	3.05	1.06	3.47×10^2

Assay conditions: Phosphate buffer (100 mM), glutathione reduced (variable), NADPH (0.4mM), EDTA (1 mM), glutathione reductase (1 unit), peroxide (1.6 mM), catalyst (80µM).

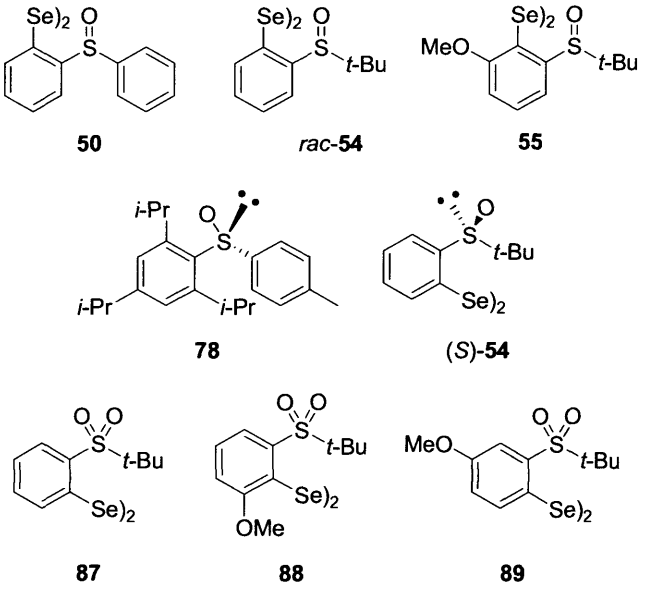
The obtained data indicate that the catalytic efficiency of the racemic sulfoxide-based diselenide *rac*-**54** is almost two times higher than that of (*S*)-**54** and ten times higher than that of Ebselen (Table 6.3). However, the huge difference between the enantioenriched and the racemic sulfoxides can not yet be explained. The catalytic activity of the sulfone-based diselenide **87** is worse than that of Ebselen and the sulfoxide-containing diselenides *rac*-**54** and (*S*)-**54**. These results are in agreement with the previously obtained data using the HPLC-based assay (Chapter 6.2.2). The significant difference between the results obtained with the sulfoxide and the sulfone-based diselenides are, however, interesting. After long reaction times the catalytic efficiencies of sulfoxides *rac*-**54** and (*S*)-**54** also

drop, presumably due to the oxidation to the sulfone by the peroxides present in the reaction mixture. It is planned to test further sulfoxide- and sulfone-containing diselenides in these assays and to establish the reaction mechanisms to explain the difference in the reactivity of compounds *rac*-**54**, (*S*)-**54** and **87.**

7. Conclusions and Perspectives

The work presented in this thesis is centred on two approaches to synthesise new effective chiral selenenylating reagents. Chapters 2 to 4 are concerned with the classical approach of using chiral diselenide precursors to generate chiral non-racemic selenium electrophiles and their reactivity.

In Chapter 2 the synthetic efforts towards several new diaryl diselenides are shown which have been used as precursors for selenium electrophiles. Heteroatoms in close proximity to the electrophilic selenium moiety, which were generated from the diselenide, can coordinate to the selenium and enhance the stereoselectivity in selenenylation reactions. Functionalities such as phosphine oxides, sulfoxides and sulfones have so far never been used in this capacity. Unfortunately, the attempted syntheses of two different kinds of phosphine-oxide-containing diselenides presented in this thesis remained unsuccessful with the chosen methods. A change in the synthetic approach (e.g. ester- or etherification of a (di)selenide with a phosphine oxide) however could in theory lead to a successful formation of this new class of chiral diselenides.



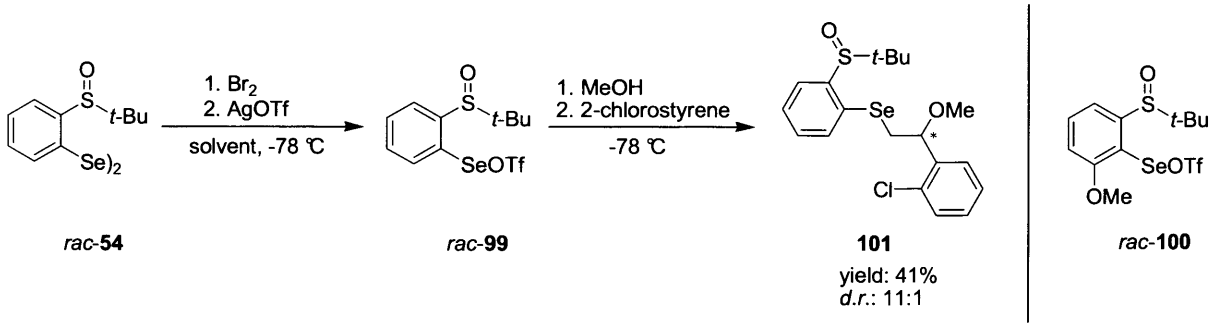
Scheme 7.1: *Successfully synthesised new diselenides*

The syntheses of several sulfoxide- and sulfone-containing aromatic diselenides were accomplished (Scheme 7.1). Diselenides *rac*-**50**, *rac*-**54** and *rac*-**55** were initially prepared as racemic mixtures to establish the general feasibility to produce these structures from commercially available starting materials in few steps. Subsequently, it was also achieved to synthesise chiral non-racemic diselenides (*R*)-**78** and (*S*)-**54** with reasonable yields via a more laborious route. A crystal structure of (*S*)-**54** has been obtained showing some interesting properties.

Besides the planned sulfoxide-containing diselenides it was also possible to synthesise several sulfone-containing diselenides (**87**, **88** and **89**). Their crystal structures were compared with (*S*)-**54**.

In all cases the introduction of the selenium atom could be realised via *ortho*-lithiation of the sulfoxides or sulfones and subsequent addition of elemental selenium to produce the corresponding selenols which are readily oxidised with air to the corresponding diselenides.

Three of the synthesised diselenides – *rac*-**54**, (*S*)-**54** and *rac*-**55** – were used as precursors for methoxyselenenylation reactions shown in Chapter 3.



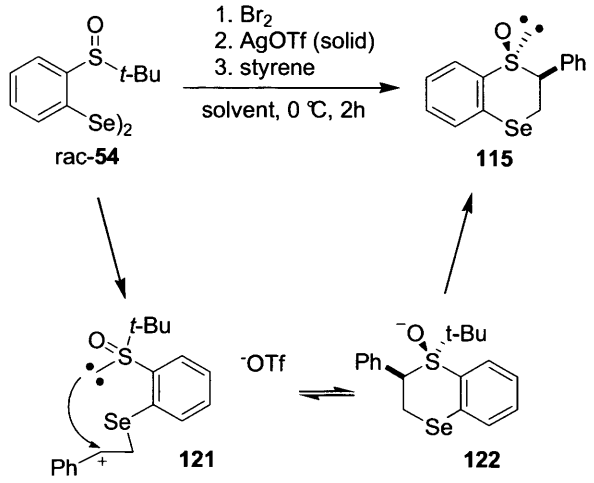
rac-**54** *rac*-**99** **101** yield: 41% *d.r.*: 11:1 *rac*-**100**

Scheme 7.2: *Selenenylation reaction with sulfoxide rac-**99***

The ability of the corresponding selenenylating reagents to influence the stereochemical outcome of these reactions was investigated using different styrene derivatives and nucleophiles using established standard conditions (Chapter 3.2). A solvent study revealed that the stereoselectivity strongly depends on the polarity of the solvent. Best results were obtained using *rac*-**99** in dichloromethane with diastereomeric ratios up to 11:1 (Scheme 7.2). It was anticipated that *rac*-**100** would show better selectivities than *rac*-**99** in these reactions, in analogy to earlier experiments by Wirth *et al.* using similar selenium electrophiles. However, the diastereomeric ratios obtained with *rac*-**100** did not exceed 2:1.

When the reaction conditions for the selenenylation reaction were slightly altered, an astonishing new reactivity of *rac*-**99** was observed, leading to products of type **115**. As detailed in Chapter 4, sulfoxides show a range of interesting reactivities as they have a significantly stronger dipole moment than carbonyl groups, with the positive charge centred on the sulfur atom. However, in the observed reactions the lone electron pair on the sulfur atom seems to act as a nucleophile. Several mechanisms

which would allow the formation of the new products **115** were discussed. Most of them could be already disproven by contradictory experimental results. So far, only the mechanism shown in Scheme 7.3 is able to explain the experimental data. The behaviour of the sulfoxides in these reactions is, if true, remarkable and could lead to other interesting heterocyclic structures using different starting materials (Chapter 4.2).



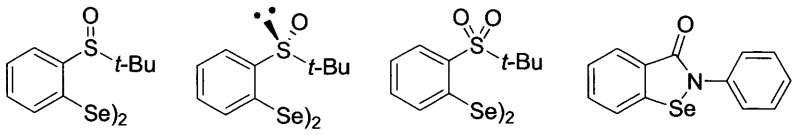
Scheme 7.3: *Cyclisation reaction using rac-**54** under altered reaction conditions*

The focus of Chapter 5 was on the second approach to generate chiral selenium electrophiles by using chiral non-racemic couteranions together with non-chiral electrophilic selenium species ($PhSe^+$). To realise this concept, based on the "Asymmetric Counteranion Directed Catalysis" (ACDC), several chiral acids and silver salts were synthesised. However, it was not possible to observe any influence on the selectivities during the selenenylation reactions using unfunctionalised selenium electrophiles. The use of functionalised selenium electrophiles did not enhance the selectivities; the enantiomeric or diastereomeric ratios remained below 3%. This was surprising taking Toste's results into account showing the successful manipulation of thiiranium ions in Chapter 5.3. Research in this area was abandoned as a successful implementation of this strategy would have needed more time. Computational methods, for example for the determination of the preferential formation of matched/mismatched ion pairs, could be beneficial for further studies in this research.

In the last chapter some of the research done in cooperation with Professor Mugesh's group in Bangalore, India, was highlighted to determine the potential of three newly synthesised diselenides as glutathione peroxidase (GPx) mimics.

Mugesh and co-workers used two different assays, an HPLC-based assay and an UV-visible spectrophotometric method, to test the efficiency of selenium compounds as GPx mimics. Both assays showed that the three tested diselenides (Scheme 7.4) can act as catalysts using different thiols and peroxides as co-substrates and substrates. It was observed that the sulfoxide-based diselenides **54** are more efficient catalysts than Ebselen and the sulfone based diselenide **87**. However, the activity of all

catalysts depended on the nature of the peroxide used. Additionally, it was observed that after long reaction times the catalytic efficiencies of sulfoxides **54** dropped, presumably due to the oxidation of the sulfoxide by the peroxides. Further sulfoxide and sulfone-based diselenides are about to be tested in these assays, to establish the reaction mechanisms and to explain the difference in the reactivity of sulfoxide- and sulfone-based compounds.



rac-**54** (*S*)-**54** **97** **215**

***Scheme** 7.4: Selenium compounds as potential GPx mimics*

In conclusion, the successfully synthesised sulfoxide-containing diselenides complement the already existing electrophilic selenium reagents, but did so far not prove to be more effective than some of the already established compounds. Although the synthesis of phosphine-oxide-containing diselenides could not be accomplished in the course of this thesis, further attempts to do so are still desirable in order to increase the overall efficiency of chiral selenenylation reactions as valuable tool for organic synthesis. Overall, it was found that the "classical" approach, using the inherit chirality of selenium electrophiles, is still a more successful attempt for stereoselective functionalisations of alkenes than the attempted use of chiral counteranions. Although the ACDC concept failed in the course of this thesis, it could still be worthwhile to examine the reasons for this failure by computational methods and find possible experimental solutions employing the computational results. The astonishing reactivity found with one of the sulfoxide-containing diselenides needs further investigation. Appropriate chiral sulfoxide precursor molecules could offer a new tool for the synthesis of chiral non-racemic sulfoxide-containing cyclic (six-membered) ring systems. Products derived by exploiting this strategy are interesting structures for agricultural, pharmaceutical and medicinal chemistry.

8. Experimental

8.1 General Methods

The reactions were carried out using standard laboratory equipment. Air and/or moisture sensitive experiments were performed under an inert atmosphere of argon and with flame dried glassware. All reactions were stirred by magnetic stirring and – when needed – warmed to defined constant temperatures by hotplates with temperature probe control in dry heating blocks or silicon oil baths. Reactions performed at low temperatures were stirred in reaction vessels in a dry ice/acetone bath (–78 °C), acetone/liquid nitrogen bath (–50 °C and –40 °C), ice/NaCl bath (–15 °C), or ice/water (0 °C). Rotary evaporators Büchi B-461, B-481 or B-490 were used for solvent evaporations (reduced pressure to 15 mbar); further drying was undertaken by the use of a high vacuum apparatus. A Büchi GKR-50 Kugelrohr distillation apparatus was employed for Kugelrohr distillations. For inert reactions, freshly over drying agents and under inert atmosphere distilled anhydrous solvents were used: THF and diethylether were dried over sodium, dichloromethane and acetonitrile were dried over CaH, cyclopentyl methylether (CPME), chloroform, methanol, ethanol, *i*-propanol and *t*-butanol were dried over 4 Å molecular sieves. Other chemicals were purchased from Acros, Aldrich, Alfa Aesar or Fluka and were used without further purification, except if indicated otherwise in the experimental procedure.

8.2 Chromatographic Methods

8.2.1 Thin Layer Chromatography

All reactions were monitored by thin-layer chromatography (TLC) which was performed on pre-coated aluminium sheets of Merck silica gel 60 F254 (0.20 mm) and visualised by UV radiation or by staining with ceric ammonium molybdate solution (235 ml distilled H_2O, 12 g ammonium molybdate, 0.5 g ceric ammonium molybdate, 15 ml concentrated sulfuric acid), phosphomolybdic acid solution

(10 g phosphomolybdic acid, 100 ml absolute ethanol), anisaldehyde solution (135 ml absolute ethanol, 5 ml concentrated sulfuric acid, 1.5 ml glacial acetic acid, 3.7 ml *p*-anisaldehyde) potassium permanganate solution (1.5 g $KMnO_4$, 10 g K_2CO_3, 1.25 ml 10% NaOH, 200 ml distilled H_2O) or iodine. For some compounds retention factors (R_f-values) are given. R_f-values are defined as the distance travelled by a compound divided by the distance travelled by the solvent. Abbreviations for used solvents are: E (diethyl ether), PE (petroleum ether), EA (ethyl acetate) and Hex (hexane).

8.2.2 Column Chromatography

Column chromatographies were performed with silica gel 60 (Merck, 230-400 mesh) under increased pressure (Flash Chromatography) or as gravitational column chromatography. The used eluting solvents are indicated in the text.

8.2.3 High Pressure Liquid Chromatography (HPLC)

For HPLC measurements was used an arrangement from Shimadzu. The Shimadzu Class VP consisted of SIL-10ADVP (auto injector), LC-10 ATVP (liquid chromatograph), FCV-10ALVP (pump), DGU-14A (degasser), CTO-10ASVP (column oven), SCL-10AVP (system controller) and a SPD-M10A (diode array detector). The only solvents used were hexane and 2-propanol (both of HPLC grade purity, Fisher Scientific). Analytical chiral columns *Chiracel® OD* (0.46 cm Ø x 25 cm), *Chiracel® OD-H* (0.46 cm Ø x 25 cm), *Chiracel® OB-H* (0.46 cm Ø x 25 cm), *Chiracel® AD* (0.46 cm Ø x 25 cm) were used for separation of enantiomers at solvent flow rates of 0.5 ml/min.

8.3 Physical Data

8.3.1 ^{1}H NMR Spectroscopy

Bruker DPX 500 (500 MHz), Bruker DPX 400 (400 MHz), Bruker DPX 250 (250 MHz)

The chemical shifts δ are given in ppm downfield of tetramethylsilane (δ = 0 ppm). Compounds and crude reaction mixtures are dissolved in either deuterated chloroform, deuterated acetone or deuterated dimethylsulfoxide. Coupling constants (*J*) are given in Hertz. The multiplicity of signals is designated: s = singlet:, d = doublet, t = triplet, q = quartet, quin = quintet, dt = doublet of triplets, td = triplet of doublets, m = multiplet. Residual solvent peaks are assigned as follows: 7.26 ppm for chloroform, 2.54 ppm for dimethylsulfoxide, 2.05 ppm for acetone. In cases of diastereomeric mixtures, the diastereomeric peaks are indicated with an asterisk (*).

8.3.2 ^{13}C NMR Spectroscopy

Bruker DPX 500 (125 MHz), Bruker DPX 400 (100 MHz), Bruker DPX 250 (62.5 MHz)

The chemical shifts δ are given in ppm downfield of tetramethylsilane (δ = 0 ppm). Compounds and crude reaction mixtures are dissolved in either deuterated chloroform, deuterated acetone or deuterated dimethylsulfoxide. Residual solvent peaks are assigned as follows: 77.36 ppm for chloroform, 40.45 ppm for dimethylsulfoxide, 29.84 ppm and 206.26 ppm for acetone. In cases of diastereomeric mixtures, the diastereomeric peaks are indicated with an asterisk (*).

8.3.3 ^{31}P NMR Spectroscopy

Bruker DPX 500 (202 MHz)

The chemical shifts δ are given in ppm. Compounds and crude reaction mixtures are dissolved in deuterated chloroform. In cases of diastereomeric mixtures, the diastereomeric peaks are indicated with an asterisk (*).

8.3.4 ^{77}Se NMR Spectroscopy

Joel Eclipse 300 (57 MHz)

The chemical shifts δ are given in ppm. Compounds and crude reaction mixtures are dissolved in deuterated chloroform but measured under "solvent free" conditions due to the configuration of the NMR. In cases of diastereomeric mixtures, the diastereomeric peaks are indicated with an asterisk (*).

8.3.5 Mass Spectrometry

Swansea: LTQ Orbitrap XL

Cardiff: Water LCR Premier XE-tof

Mass spectrometric measurements have been performed by the EPSRC Mass Spectrometry Service Centre, Swansea University or by R. Jenkins/R. Hicks/D. Walker at Cardiff University. Ions were generated by the atmospheric pressure ionisation techniques voltage applied corana discharge pin (APCI), Electrospray (ES) or Electron Ionisation (EI). Mass fragments usually are in atomic mass units per elementary charges (m/z) with relative abundance of ion in percentage (%). The high resolution mass spectrometry (HRMS) for most of the compounds was carried out at EPSRC Mass Spectrometry Service Centre, Swansea University. The molecular ion peaks values quoted for either

molecular ion (M^+), molecular ion plus hydrogen ($M+H^+$) or molecular ion peaks plus ammonium ion ($M+NH_4^+$) or molecular ion plus sodium ($M+Na^+$).

8.3.6 IR Spectroscopy

IR spectra were recorded on either a Perkin Elmer 1600 series FTIR or a PC supported JASCO FT/IR 660 plus with "Spectra Manager for Windows 95/NT", Version 1.53.01 from JASCO Cooperation.

Wavenumbers are quoted in cm^{-1}. Crystalline compounds were measured as KBr disk, non-crystalline samples were measured as neat film between NaCl disks.

8.3.7 Melting Points

Melting Points were measured using a Gallenkamp variable heater with samples in open capillary tubes. All melting points are uncorrected.

8.3.8 Optical Rotation

The optical rotation of compounds was measured at 20 °C in cuvettes of 50 mm length with an AA-1000 Polarimeter from Optical Activity LTD.

8.3.9 X-Ray Crystallography

Bruker CCD diffractometer with graphite-monochromatised Mo-K_α radiation (λ = 0.71073 Å)

X-Ray crystallographic studies were carried out at the X-Ray Crystallography Service at Cardiff University or at the EPSRC X-Ray Crystallography Service Centre, Southampton. Single crystals were mounted at room temperature on the ends of glass fibers and data were collected at room temperature (291 K). The structures were solved by direct methods and refined using the SHELXTL software package. In general, all non-hydrogen atoms were refined anisotropically. Hydrogen atoms were assigned at idealized locations. The structure was solved by a direct method and refined by a full-matrix least-squares procedure on F^2 for all reflections (SHELXL-97).

8.4 General Procedures

GP 1: General procedure for the synthesis of diselenides from bromo-precursors:

The bromo precursor (2 mmol) was dissolved in dry THF (20 ml) under argon, cooled to –78 °C, and *t*-butyllithium (6 mmol, 1.7 M solution in hexanes) was added dropwise. After the mixture had been warmed up to 0 °C and stirred for 60 min, selenium powder (2.2 mmol) was added. The mixture was allowed to warm up to room temperature and was stirred for an additional 3 h, 1 M HCl (20 ml) was then added. After extraction of the resulting mixture with diethyl ether (3 x 25 ml) and drying of the combined organic phases with $MgSO_4$, powdered KOH (100 mg) was added. After filtration, the solvent was removed under reduced pressure and the residue purified by flash chromatography on silica gel. The diselenides were obtained as yellow oils.

GP 2: General procedure for the synthesis of diselenides from phenyl precursors by *ortho*-lithiation:

To a solution of phenyl sulfoxide or phenyl sulfone (13 mmol) in dry THF (130ml), *n*-butyllithium (2.5 M solution in hexane, 14.3 mmol, 5.72 ml) was added slowly at –78 °C. The mixture was stirred for 1.5 h at this temperature. Then selenium (14.3 mmol, 1.13 g) was added with vigorous stirring at 0 °C. After 15 h stirring at room temperature the mixture was quenched with water (100 ml) and extracted with dichloromethane (3 x 100 ml). The combined organic phases were treated with powdered KOH (600 mg) and dried with $MgSO_4$. After vigorous stirring for 30 min at r.t. and filtration, the solvent was removed under reduced pressure. The crude yellow or orange products were purified with silica gel chromatography.

GP 3: General procedure for the addition of selenium electrophiles to styrene:

The diselenide (0.1 mmol) was dissolved in dry solvent (4 ml) under argon, cooled to –78 °C, and bromine (0.1 mmol, 0.1 ml of a 1 M solution in CCl_4) was added. After 20 min, silver triflate (solid) (54 mg, 0.21 mmol) was added and the mixture was stirred for 25 min at –78 °C. To the reaction mixture was added MeOH (0.10 ml) and subsequently the alkene (0.22 mmol). After the mixture had been stirred for 2 h at –78 °C, it was warmed to 0 °C and further stirred for 30 min. Then 2,4,6-collidine (0.10 ml) was added, followed by water (4 ml). After extraction of the reaction mixture with dichloromethane (3 x 10 ml) the combined organic phases were dried with $MgSO_4$ and the solvent removed under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate/hexane, 5:1), giving the addition products as colourless oils. The diastereomers were not separated during this procedure.

GP 4: General procedure for the synthesis of 1,4-benzoselenothiine-1-oxides:

The diselenide (0.1 mmol) was dissolved in dry solvent (4 ml) under argon, cooled to –78 °C, and treated with bromine (0.1 mmol, 0.1 ml of a 1 M solution in CCl_4). After 20 min silver triflate (solid) (54 mg, 0.21 mmol) was added and the mixture was stirred for 25 min at –78 °C. To the reaction mixture alkene (0.22 mmol) was added and it was stirred for 5 min at –78 °C. Then it was immediately warmed to 0 °C and further stirred for 60 min. MeOH (0.10 ml) was added and the mixture was stirred for additional 10 min at 0 °C. Then saturated $NaHCO_3$ solution (5 ml) was added and the layers separated. The aqueous layer was washed with dichloromethane (3 x 10 ml) and the combined organic layers were dried with Na_2SO_4, filted the solvent was removed under reduced pressure. The residue was purified by flash column chromatography (ethyl acetate/hexanes 1:5) on neutral Al_2O_3, yielding the addition products as pale yellow oils.

GP 5: General procedure for the cleavage of menthyl esters with KOH:

To a solution of potassium hydroxide (65.5 mmol, 3.67 g) in a 1:1 mixture of water and ethanol (14 ml), 7,7'-bis-(*L*-menthyloxy-carbonyloxy)-1,1'-spirobiindane (324.5 mg, 0.55 mmol) was added. The mixture was heated to reflux for 60 min and was then cooled to room temperature. The solvent was removed under reduced pressure and the residue was dissolved in 20 ml of a 1:1 mixture of water and hexane. The layers were separated and the aqueous layer was acidified with 6 M HCl. The resulting white precipitate was extracted with a mixture (10 ml) of hexane and ethyl acetate (9:1). The organic layer was dried with $MgSO_4$, filtrated and the solvent was removed under reduced pressure.

GP 6: General procedure for the reaction of chiral silver salts with selenenylating reagents:

The diselenide (0.1 mmol) was dissolved in dry solvent (4 ml) under argon, cooled to –78 °C and treated with bromine (0.1 mmol, 0.1 ml of a 1M solution in CCl_4). After 15 min a solution of the chiral silver salt (0.22 mmol) in 0.2 ml dichloromethane was added and stirred for 30 min at –78 °C. Then the alkene was added and the mixture was further stirred at –78 °C for 10 min and warmed to room temperature. Stirring was continued for 4 h. 2,4,6-Collidine (0.05 ml) and water (4 ml) were added, the layers separated and the aqueous layer extracted with dichloromethane (3 x 8 ml). After drying the combined organic layers with $MgSO_4$, filtration and removal of the solvent under reduced pressure, the residue was purified by flash chromatography on silica gel.

GP 7: General procedure for the reaction of chiral acids with selenenylating reagents:

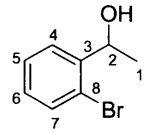
To a solution of the diselenide (0.1 mmol) in dry solvent (4 ml) under argon at –78 °C was added bromine (0.1 mmol, 0.1 ml of a 1M solution in CCl_4) and the mixture is stirred for 15 min. Then Ag_2CO_3 (0.22 mmol) was added and the solution was further stirred for 10 min. This was followed by the addition of the chiral silver salt (0.22 mmol) and further stirring for 20 min at –78 °C. Then the

alkene (0.25 mmol) was added and the mixture was stirred for 10 min at –78 °C and 4 h at room temperature. 2,4,6-Collidine (0.05 ml) and water (4 ml) were added, the layers separated and the aqueous layer extracted with dichloromethane (3 x 8 ml). The combined organic layers were dried with $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel.

8.5 Characterisation of Compounds

8.5.1 Chiral Diselenides

8.5.1.1 *rac*-1-(2-Bromophenyl)ethanol (21)[26]



2'-Bromoacetophenone (2.5 mmol, 498 mg, 337 µl) was dissolved in dry ethanol (20 ml) under argon and cooled to 0 °C. Sodium borohydride (10.0 mmol, 378 mg) was added in one portion and the stirring was continued at 0 °C for 30 min. The mixture was stirred additionally for 5 h at room temperature, then saturated NH_4Cl solution (15 ml) was added and most of the ethanol removed under reduced pressure. After extraction of the resulting mixture with diethyl ether (3 x 15 ml), drying of the combined organic phases with Na_2SO_4 and filtration, the solvent was removed under reduced pressure. The residue was purified by column chromatography (diethyl ether/petrol ether 1:5) on silica gel, to afford *rac*-1-(2-bromophenyl)ethanol (450 mg, 89.6%, 2.24 mmol) as colourless oil. The obtained spectroscopic data are in agreement with literature data.

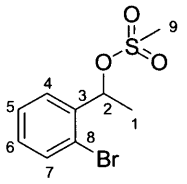
R_f (EA/Hex 1:3) = 0.60.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 8.0 Hz, 1H, C*H*-7), 7.44 (d, *J* = 8.0 Hz, 1H, C*H*-4), 7.27 (t, *J* = 8.0 Hz, 1H, Ar*H*), 7.06 (t, *J* = 8.0 Hz, 1H, Ar*H*), 5.16 (q, *J* = 6.5 Hz, 1H, C*H*-2), 1.40 (d, *J* = 6.5 Hz, 3H, CH_3-1) ppm.

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 144.6 (*C*-3), 132.7 (Ar*C*), 128.8 (Ar*C*), 127.9 (Ar*C*), 126.7 (Ar*C*), 121.7 (Ar*C*), 69.2 (*C*HOH-2), 23.6 (*C*H_3-1) ppm.

C_8H_9BrO: 201 g/mol

8.5.1.2 *rac*-1-(2-Bromophenyl)ethyl methanesulfonate (22)



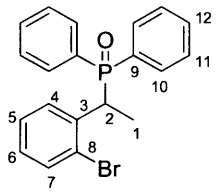
rac-1-(2-Bromophenyl)ethanol (1.50 mmol, 303 mg) was dissolved in dry dichloromethane (6 ml) under argon and cooled to 0 °C. Methanesulfonyl chloride (1.60 mmol, 183 mg, 124 µl) and triethylamine (1.6 mmol, 162 mg, 222 µl) added dropwise and the stirring was continued at 0 °C for 15 min. The mixture was stirred additional 25 h at room temperature, then a 1 M HCl solution (6 ml) was added. After extraction of the resulting mixture with diethyl ether (3 x 6 ml), the combined organic layers were washed subsequently with aqueous saturated $NaHCO_3$ (3 x 6 ml) and brine (3 x 6 ml) and dried with Na_2SO_4, The solvent was removed under reduced pressure and the crude product (419 mg, 1.5 mmol) used without further purification.

R_f (E/PE 1:1) = 0.33.

Crude product oil: **^{1}H NMR** (250 MHz, $CDCl_3$): δ = 7.46–7.51 (m, 2H, Ar*H*), 7.32 (t, *J* = 6.5 Hz, 1H, Ar*H*), 7.08–7.14 (m, 1H, Ar*H*), 6.14 (q, *J* = 4.5 Hz, 1H, C*H*-2), 2.80 (s, 3H, C*H*$_3$-9), 1.65 (d, *J* = 4.5 Hz, 3H, C*H*$_3$-1) ppm.

$C_9H_{11}BrO_3S$: 279 g/mol

8.5.1.3 *rac*-(1-(2-Bromophenyl)ethyl)diphenylphosphine oxide (24)



Diphenyl phosphine (1.50 mmol, 279.3 mg, 260 µl) was dissolved in dry THF (6 ml) under argon and cooled to 0 °C, then *n*-butyllithium (1.50 mmol, 2.5 M solution in hexane, 600 µl) was added dropwise and the solution was stirred at 0 °C for 30 min. 1-(2-Bromophenyl)ethyl methanesulfonate (1.5 mmol, 418.5 mg) was dissolved in dry THF (6 ml) under argon, cooled to 0 °C and added dropwise to the solution of lithium diphenylphosphine. The mixture was stirred for 1 h at 0 °C, then warmed to room temperature and stirred for an additional hour. Then water (6 ml) was added and the resulting mixture extracted with diethyl ether (3 x 6 ml). The combined organic layers were washed with water (3 x 10 ml) and dried with Na_2SO_4. After filtration, the solvent was removed under reduced pressure and the residue was purified by column chromatography (dichloromethane) on silica gel, giving the title compound as colourless oil in 34% yield (195 mg, 0.51 mmol) over 3 steps from *rac*-1-(2-bromophenyl)ethanol.

R_f (CH_2Cl_2/acetone 10:1) = 0.25.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.93–7.99 (m, 3H, Ar*H*), 7.52–7.58 (m, 3H, Ar*H*), 7.45–7.50 (m, 2H, Ar*H*), 7.36 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.24–7.33 (m, 2H, Ar*H*), 7.19–7.23 (m, 2H, Ar*H*), 6.97–7.92 (m, 1H, Ar*H*), 4.26–4.35 (m, 1H, C*H*-2), 1.52 (dd, *J* = 7.3 Hz, *J* = 15.7 Hz, 3H, CH_3-1) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.1 (d, $J_{C\text{-}P}$ = 4 Hz, Ar*C*), 132.3 (Ar*C*), 131.5 (d, $J_{C\text{-}P}$ = 2 Hz, $J_{C\text{-}P}$ = 56 Hz, Ar*C*), 131.1 (d, $J_{C\text{-}P}$ = 9 Hz, Ar*C*), 130.7 (d, $J_{C\text{-}P}$ = 9 Hz, Ar*C*), 130.4 (d, $J_{C\text{-}P}$ = 4 Hz, Ar*C*), 128.7 (d, $J_{C\text{-}P}$ = 11 Hz, Ar*C*), 127.9 (d, $J_{C\text{-}P}$ = 11 Hz, Ar*C*), 128.1 (d, $J_{C\text{-}P}$ = 68 Hz, Ar*C*), 124.8 (d, $J_{C\text{-}P}$ = 9 Hz, Ar*C*), 38.6 (d, $J_{C\text{-}P}$ = 68 Hz, *C*H-2), 15.5 (d, $J_{C\text{-}P}$ = 3 Hz, *C*H_3-1) ppm.

^{31}P NMR (202 MHz, $CDCl_3$): δ = 34.0 ppm.

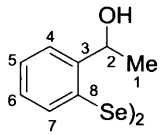
MS (ESI+) m/z (%): 387 ([M+H^+], 100), 385 ([M+H^+], 98), 307 (2).

HRMS (ESI+): $[M+H]^+$ calculated for $C_{20}H_{19}BrOP$: 385.0351, found: 385.0351.

IR (film): $\tilde{\nu}$ = 3058, 2973, 2930, 2872, 1590, 1472, 1438, 1311, 1182, 1117, 1072, 1047, 1019, 998, 927, 800, 754, 721, 709, 694, 660, 604, 545 cm^{-1}.

$C_{20}H_{18}BrOP$: 385 g/mol

8.5.1.4 *rac*-Bis[(1-hydroxyethyl)phenyl diselenide (26)[72]



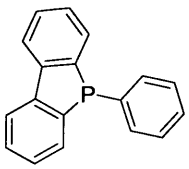
Synthesised according to GP 1 with 1.01 g (5 mmol) *rac*-1-(2-bromophenyl)ethanol, *t*-butyllithium (15 mmol, 10 ml, 2.5 M solution in hexanes) and selenium (435 mg, 5.5 mmol). After column chromatography (hexane/ethyl acetate 4:1→1:4), the product was isolated with 24% yield (470 mg, 1.16 mmol) as yellow oil. The obtained spectroscopic data are in agreement with literature data.

R_f (E/PE 1:1) = 0.21.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 7.5 Hz, 2H, C*H*-7), 7.52 (d, *J* = 7.3 Hz, 2H, C*H*-4), 7.33 (m, 2H, Ar*H*), 7.21 (m, 2H, Ar*H*), 5.07 (m, 2H, C*H*-2), 2.10 (br s, 2H, O*H*), 1.38 (d, *J* = 6.5 Hz, 6H, CH_3-1) ppm.

$C_{16}H_{18}O_2Se_2$: 400 g/mol

8.5.1.5 (2,2'-Bisphenylylene)phenylphosphine (29)[31]



To a stirred solution of triphenylphosphine oxide (5.00 mmol, 1.39 mg) in 40 ml THF at 0 °C under argon atmosphere phenyllithium (15 mmol, 2.0 M solution in dibutylether, 7.5 ml) was added. The mixture was refluxed for 15 h. After hydrolysis with water (20 ml), the solvent was removed under reduced pressure. To the residue water (20 ml) was added and the mixture was neutralized with 1 M HCl, extracted with dichloromethane (3 x 20 ml). The combined organic phases were dried with anhydrous $MgSO_4$, filtrated and the solvent was removed under reduced pressure. The residue was purified by column chromatography (silica gel; hexane/ethyl acetate 4:1) to give (2,2'-biphenylylene)phenylphosphine in 50% yield (650 mg, 2.5 mmol) as ivory coloured crystals. The obtained spectroscopic data are in agreement with literature data.

R_f (E/PE 1:1) = 0.58.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, J = 8.0 Hz, 3H), 7.77–7.71 (m, 2H), 7.48 (t, J = 8.0 Hz, 2H), 7.36–7.32 (m, 4H), 7.30–7.23 (m, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.7 (d, $J_{C\text{-}P}$ = 3 Hz, Ar*C*), 142.6 (d, $J_{C\text{-}P}$ = 3 Hz, Ar*C*), 136.2 (d, $J_{C\text{-}P}$ = 18 Hz, Ar*C*), 132.8, (d, $J_{C\text{-}P}$ = 20 Hz, Ar*C*), 130.6 (d, $J_{C\text{-}P}$ = 20 Hz, Ar*C*), 129.3, 128.7 (d, $J_{C\text{-}P}$ = 4 Hz, Ar*C*), 128.7, 127.7 (d, $J_{C\text{-}P}$ = 6 Hz, Ar*C*), 121.4 ppm.

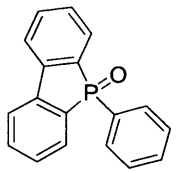
^{31}P NMR (202 MHz, $CDCl_3$): δ = –10.0 ppm.

MS (EI+) m/z (%): 260 (M^+,100), 228 (15), 183 (48), 152 (12), 139 (3), 129 (2), 107 (2), 77 (100), 74 (15), 63 (3), 51 (50), 50 (25).

M.P.: 91–92 °C.

$C_{18}H_{13}P$: 260 g/mol

8.5.1.6 (2,2'-Bisphenylylene)phenylphosphine oxide (30)[31]



To a solution of (2,2'-biphenylylene)phenylphosphine (2.20 mmol, 572 mg) in acetic acid (60 ml), 30% aqueous hydrogen peroxide (0.033 ml) was added. The mixture was stirred at room temperature for 3 h, and the solvent was removed under reduced pressure. The residue was dissolved in dichloromethane (60 ml) and washed with saturated aqueous sodium hydrogen carbonate (3 x 30 ml) and brine (2 x 30 ml). The organic layer was dried with anhydrous $MgSO_4$, then filtrated and the solvent was removed under reduced pressure. The residue was recrystallised from ethyl acetate to give (2,2'-biphenylylene)phosphine oxide as colourless crystals in 60% (364 mg, 1.32 mmol) yield. The obtained spectroscopic data are in agreement with literature data.

R_f (EA/Hex 1:4) = 0.01.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.77–7.74 (m, 2H), 7.68–7.48 (m, 6H), 7.42–7.39 (m, 1H), 7.32–7.29 (m, 4H) ppm.

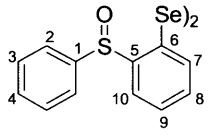
^{13}C NMR (125 MHz, CDCl3): δ = 141.7 (d, $J_{C\text{-}P}$ = 22 Hz, Ar*C*), 133.3 (Ar*C*H), 132.5 (Ar*C*H), 132.1 (d, $J_{C\text{-}P}$ = 3 Hz, Ar*C*), 131.0 (d, $J_{C\text{-}P}$ = 11 Hz, Ar*C*H), 130.8 (d, $J_{C\text{-}P}$ = 103 Hz, Ar*C*), 129.9 (d, $J_{C\text{-}P}$ = 10 Hz, Ar*C*H), 129.4 (d, $J_{C\text{-}P}$ = 11 Hz, Ar*C*H), 128.7 (d, $J_{C\text{-}P}$ = 11 Hz, Ar*C*H), 121.2, (d, $J_{C\text{-}P}$ = 10 Hz, Ar*C*H), ppm.

^{31}P NMR (202 MHz, $CDCl_3$): δ = 33.8 ppm.

M.P.: 158–160 °C.

$C_{18}H_{13}OP$: 276 g/mol

8.5.1.7 *rac*-Bis-[2-(phenylsulfinyl)phenyl] diselenide (50)



To a solution of diisopropylamine (11.0 mmol, 1.54 ml) in dry tetrahydrofuran (20 ml) under argon, *n*-butyllithium (10.0 mmol, 4.40 ml, 2.25 M solution in hexane) was added at 0 °C and stirred for 15 min. This lithium diisopropylamide (10.0 mmol) solution was added to a solution of diphenylsulfoxide (5.00 mmol, 1.01 g) in dry tetrahydrofuran (30 ml) under argon at –78 °C. The mixture was stirred for 3 h at –78 °C then warmed to 0 °C and selenium (0.435 mg, 5.50 mmol) was added in one portion with vigorous stirring. The resulting bright yellow solution was warmed to room temperature and stirred over night. To this mixture, 1 M HCl (15 ml) was added and the layers were separated. The aqueous layer was washed with diethyl ether (3 x 10 ml) and the combined organic layers were treated with grounded KOH (200 mg) and dried with Na_2SO_4. After filtration, the solvent was removed under reduced pressure and column chromatography (hexane/ethyl acetate 1:2) afforded the diselenide in 13% yield (364 mg, 0.65 mmol) as a yellow oil.

R_f (EA/Hex 2:1) = 0.20.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.90 (dd, *J* = 1.1 Hz, *J* = 7.7 Hz, 2H, *H*-7), 7.64–7.70 (m, 4H), 7.46–7.54 (m, 4H), 7.41–7.45 (m, 6H), 7.24–7.32 (m, 2H) ppm.

^{13}C NMR (63 MHz, CDCl3): δ = 146.6 (*C*-6), 144.4, 134.4, 131.9, 131.3, 129.3, 129.2, 128.5, 126.1, 125.7 ppm.

^{77}Se NMR (57 MHz, $CDCl_3$): δ = 440, 439* ppm.

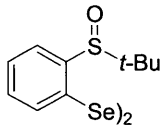
MS (ES+) m/z (%): 1145 $[2M+NH_4]^+$, 15), 585 (15), 563 ($[M+H]^+$, 100), 483 (23), 391 (12), 315 (4), 279 (13).

HRMS (ES+): $[M+H]^+$ $C_{24}H_{19}O_2S_2{}^{76}Se_2$ calculated 555.9200; found 555.9215.

IR (film): $\tilde{\nu}$ = 3055, 2238, 1567, 1475, 1442, 1088, 1049, 1017, 998, 911, 747, 686, 645 cm^{-1}.

$C_{24}H_{18}O_2S_2Se_2$: 560 g/mol

8.5.1.8 *rac*-Bis-[2-(*t*-butylsulfinyl)phenyl] diselenide (*rac*-54)



Synthesised according to GP 2 with 3.30 g (18.1 mmol) *rac*-1-(*t*-butylsulfinyl)benzene, *n*-butyllithium (19.9 mmol, 7.96 ml, 2.5 M solution in hexanes) and selenium (1.57 g, 19.9 mmol). After column chromatography (hexane/ethylacetate 4:1→1:4), the racemic product was isolated with 39% (3.67 g, 7.06 mmol) yield as yellow oil which crystallized from diethyl ether upon standing.

R_f (EA/Hex 1:1) = 0.10.

Diastereomeric peaks are indicated with an asterisk (*), *d.r.*: 1:1.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (t, *J* = 12.0 Hz, 4H, Ar*H*), 7.30 (d, *J* = 8.0 Hz, 4H, Ar*H*), 1.20 (s, 9H, $C(CH_3)_3$), 1.19 (s, 9H, $C(CH_3)_3$)* ppm.

^{13}C NMR (126 MHz, $CDCl_3$): δ = 140.8 (*C*), 140.8* (*C*), 132.7 (*C*H), 132.4 (*C*H), 132.2 (*C*), 132.2* (*C*), 127.7 (*C*H), 127.7* (*C*H), 127.5 (*C*H), 127.5* (*C*H), 58.6 ($C(CH_3)_3$), 58.6* ($C(CH_3)_3$), 23.3 ($C(CH_3)_3$) ppm.

^{77}Se NMR (57 MHz, $CDCl_3$): δ = 438, 440* ppm.

IR (film): $\tilde{\nu}$ = 2962, 2925, 2235, 1569, 1471, 1455, 1439, 1362, 1168, 1127, 1045, 1018, 921, 755, 731 cm^{-1}.

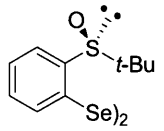
MS (ES+): m/z (%): 544 (15), 523 ($[M+H]^+$,100), 497 (43), 462 (23), 449 (30), 423 (15), 391 (17), 279 (22), 260 (47), 235 (22), 205 (30), 187 (13).

HRMS (ES+): $[M+H]^+$ $C_{20}H_{27}O_2S_2{}^{76}Se_2$ calculated 514.9831; found 514.9829.

M.P.: 115–116 °C (crystals from diethyl ether).

$C_{20}H_{26}S_2O_2Se_2$: 520 g/mol.

8.5.1.9 (*S*)-(–)-Bis[2-(*t*-butylsulfinyl)phenyl] diselenide [(*S*)-54]



Synthesised according to GP 2 with 320 mg (1.76 mmol) (–)-(*S*)-*t*-butylphenyl sulfoxide, *n*-butyllithium (1.94 mmol, 776 µl, 2.5 M solution in hexanes) and selenium (153 mg, 1.94 mmol). After column chromatography (hexane/ethylacetate 4:1→1:4) the diselenide, was isolated with 39% yield (357 mg, 0.69 mmol) as yellow oil which crystallized from diethyl ether upon standing.

R_f (EA/PE 3:1) = 0.20.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.64 (dd, *J* = 1.3 Hz, *J* = 7.7 Hz, 2H, Ar*H*), 7.61 (dd, *J* = 1.6 Hz, *J* = 7.5 Hz, 2H, Ar*H*), 7.32 (dt, *J* = 1.4 Hz, *J* = 7.5 Hz, 2H, Ar*H*), 7.28 (dt, *J* = 1.7 Hz, *J* = 7.5 Hz, 2H, Ar*H*), 1.20 (s, 18H, C(CH_3)$_3$] ppm.

^{13}C NMR (126 MHz, $CDCl_3$): δ = 140.9 (*C*), 132.4 (*C*H), 132.2 (*C*H), 131.3 (*C*), 127.7 (*C*H), 127.5 (*C*H), 58.6 (*C*(CH$_3$)$_3$), 23.3 (C(*C*H$_3$)$_3$) ppm.

^{77}Se NMR (57 MHz, $CDCl_3$): δ = 436 ppm.

IR (KBr): $\tilde{\nu}$ = 2960, 1568, 1440, 1362, 1167, 1081, 1047, 1018, 756 cm^{-1}.

MS (ES+): m/z (%): 526 (30), 523 ([M+H]$^+$, 100), 519 (50), 515 (3), 263 (17), 261 (100), 259 (44), 257 (17), 207 (17), 205 (95), 203 (42), 201 (17).

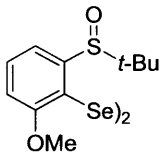
HRMS (ES+): [M+H]$^+$ calculated for $C_{20}H_{27}O_2S_2{}^{74}Se^{76}Se$: 512.9864; found 512.9864.

$[\alpha]_{20}^{D}$ = –65.5 (c = 0.11, CH_2Cl_2);

M.P.: 118.5–119.5 °C (crystals from diethyl ether).

$C_{20}H_{26}S_2O_2Se_2$: 520 g/mol.

8.5.1.10 *rac*-Bis-[2-(*t*-butylsulfinyl)-6-methoxyphenyl] diselenide (55)



Synthesised according to GP 2 with 600 mg (2.80 mmol) *rac*-1-(*t*-butylsulfinyl)-3-methoxybenzene, *n*-butyllithium (3.20 mmol, 1.28 ml, 2.5 M solution in hexanes) and selenium (225 mg, 2.85 mmol). After column chromatography (hexane/ethyl acetate 1:4), the racemic product was isolated with 24% yield (390 mg, 0.67 mmol) as yellow foam.

R_f (EA) = 0.25.

Diastereomeric peaks are indicated with an asterisk (*), *d.r.*: 1:1.

^{1}H NMR (400 MHz, $CDCl_3$): δ =7.51 (t, *J* = 7.8 Hz, 2H, Ar*H*), 7.49 (t, *J* = 7.8 Hz, 2H, Ar*H*)*, 7.43 (dd, *J* = 1.1, *J* = 7.8 Hz, 2H, Ar*H*), 7.40 (dd, *J* = 1.1, *J* = 7.8 Hz, 2H, Ar*H*)*, 7.01 (dd, *J* = 1.0, *J* = 8.1 Hz, 2H, Ar*H*), 6.98 (dd, *J* = 0.9, *J* = 8.1 Hz, 2H, Ar*H*)*, 3.71 (s, 6H, OCH_3), 3.70 (s, 6H, OCH_3)*, 1.19 (s, 18H, C(CH_3)$_3$), 1.12 (s, 18H, C(CH_3)$_3$)* ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.9* (*C*), 159.7 (*C*), 146.4* (*C*), 146.1 (*C*), 130.7* (*C*H), 130.5 (*C*H), 120.3 (*C*), 119.1* (*C*H), 119.0 (*C*H), 113.1* (*C*H), 113.0 (*C*H), 58.3*, 57.8, 56.5*, 56.4, 23.5* (C(*C*H$_3$)$_3$), 23.3 (C(*C*H$_3$)$_3$) ppm.

^{77}Se NMR (57 MHz, $CDCl_3$): δ = 378 ppm.

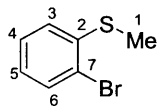
IR (film): $\tilde{\nu}$ = 2965, 2934, 1699, 1567, 1456, 1429, 1263, 1181, 1160, 1040, 785, 725 cm^{-1}.

MS (ES+) *m/z* (%): 1180 ([2M+NH_4]$^+$, 17), 583 ([M+H]$^+$, 100), 503 (15), 291 (58), 235 (38).

HRMS (ES+): [M+H]$^+$ calculated for $C_{22}H_{31}S_2O_4{}^{74}Se\,{}^{76}Se$: 573.0075, found: 573.0078.

$C_{22}H_{30}O_4S_2Se_2$: 580 g/mol.

8.5.1.11 (2-Bromphenyl)(methyl)sulfone (59)[137]



To a solution of 2-bromothiophenol (15.0 mmol, 1.81 ml) and dimethyl sulfate (19.7 mmol, 1.86 ml) a 20% solution of sodium hydroxide in water (5 ml) was slowly added. The reaction mixture was refluxed for 4 h at 110 °C and then allowed to cool to room temperature. Water (2 ml) was added and the aqueous solution was extracted with diethyl ether (3 x 7 ml). The combined organic layers were dried with Na_2SO_4 and filtrated. The solvent was removed under reduced pressure and the product was obtained in 98% (2.95 g, 14.7 mmol) yield as a slightly orange coloured liquid, which was used without further purification. The obtained spectroscopic data are in agreement with literature data.

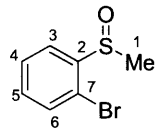
R_f (E/PE 1:1) = 0.65.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 8.0 Hz, 1H, C*H*-6), 7.31 (t, *J* = 8.0 Hz, 1H, C*H*-4), 7.12 (d, *J* = 8.0 Hz, 1H, C*H*-3), 7.01 (t, *J* = 8.0 Hz, 1H, C*H*-5), 2.48 (s, 3H, CH_3-1), ppm.

^{13}C NMR (62 MHz, $CDCl_3$): δ = 139.7 (*C*-2), 132.7 (*C*H-6), 127.8(*C*H-3), 125.7 (*C*H-4), 125.4 (*C*H-5), 121.8 (*C*-7), 15.7 (*C*H$_3$-1) ppm.

C_7H_7BrS: 201 g/mol

8.5.1.12 *rac*-1-Bromo-2-(methylsulfinyl)benzene (60)[50a]



To a solution of sodium(meta)periodate (4.05 mmol, 866 mg) in water (15 ml), THF (5 ml) and (2-bromphenyl)(methyl)sulfane (3.00 mmol, 612 mg) were added. The mixture was stirred in an open flask over night at room temperature. Then dichloromethane (20 ml) was added and the layers separated. The aqueous layer was washed with dichloromethane (3 x 10 ml) and the combined organic layers were treated with activated carbon, dried with Na_2SO_4 and filtered off. The solvent was removed under reduced pressure. 1-Bromo-2-(methylsulfinyl)benzene was obtained with 97% yield (637 mg, 2.91 mmol) as a slightly orange coloured liquid, which was used without further purification. The obtained spectroscopic data are in good agreement with literature data.

R_f (E/PE 1:1) = 0.20.

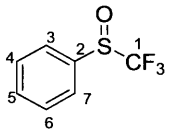
^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 8.0 Hz, 1H, C*H*-6), 7.59–7.63 (m, 2H, C*H*-3, C*H*-4), 7.39 (t, *J* = 8.0 Hz, 1H, C*H*-5), 2.83 (s, 3H, CH_3-1) ppm.

^{13}C NMR (62 MHz, $CDCl_3$): δ = 145.4 (*C*-2), 132.9 (*C*H-5), 132.3 (*C*H-6), 128.8 (*C*H-4), 125.7 (*C*H-3), 118.4 (*C*-7), 41.9 (*C*H_3-1) ppm.

IR (film): $\tilde{\nu}$ = 3050, 2980, 2910, 1570, 1443, 1426, 1247, 1107, 1090, 1060, 1016, 955 cm^{-1}.

C_7H_7BrSO: 219 g/mol

8.5.1.13 1-(Trifluoromethylsulfinyl)benzene (63)[65]



To a stirred solution of phenyl trifluoromethyl sulfide (5.5 mmol, 0.98 g) in dry dichloromethane (40 ml) at 0 °C under argon, *m*-chloroperbenzoic acid (7.20 mmol, 1.24 g) was added in small portions. After the mixture was stirred for 10 h at 0 °C, and then for 1 h at r.t. the solution was filtered and evaporated. The residue was subjected to silica gel column chromatography using a mixture of ethyl acetate/hexane (30:1) to give the product in 31% yield (0.33 g, 1.71 mmol). The obtained spectroscopic data are in agreement with literature data.

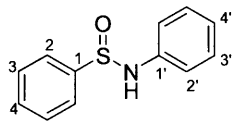
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 7.6 Hz, 2H, C*H*-3), 7.57–7.67 (m, 3H, C*H*-4, C*H*-5) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.5 (*C*-1), 130.7 (*C*H-4), 129.8 (*C*H-3), 125.8 (*C*H-2), 119.6 (q, $J_{C\text{-}F}$ = 250 Hz, *C*F_3) ppm.

MS (ES+) m/z (%): 194 ($[M+H]^+$, 8), 178 (5), 125 (100), 109 (10), 97 (28), 88 (13), 77 (35), 70 (25, CF_3), 61 (33).

$C_7H_5F_3SO$: 194 g/mol

8.5.1.14 *rac*-*N*-Phenylbenzenesulfinamide (66)[66]



To a solution of phenylmagnesium bromide (3.3 mmol, 3 M solution in diethyl ether, 1.1 ml) in dry diethyl ether (10 ml), thionylaniline (3.00 mmol, 418 mg, 338 µl) dissolved in dry diethyl ether (10 ml) was added at 0 °C. The product precipitated immediately and was hydrolysed with 10% ammonium chloride solution (10 ml). The layers were separated and the aqueous layer was washed with dichloromethane (3 x 10 ml). The combined organic layers were dried with Na_2SO_4, filtrated and the solvent was removed under reduced pressure. After column chromatography (hexane/ethyl acetate 1:2) *N*-phenylbenzenesulfinamide was obtained with 61 % yield (397 mg, 1.83 mmol) yield as an ivory coloured solid. The obtained spectroscopic data are in agreement with literature data.

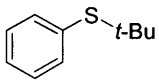
R_f (EA/Hex 1:3) = 0.15.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78–7.82 (m, 2H), 7.52–7.56 (m, 3H), 7.27–7.32 (m, 2H), 7.05–7.13 (m, 3H), 6.13 (s, 1H, N*H*) ppm.

^{13}C NMR (62 MHz, d^6-acetone): δ = 146.5 (*C*-1), 142.9 (*C*-1'), 131.8 (*C*H-4), 130.0, 129.8, 126.4, 123.5 (*C*H-4'), 119.4 (*C*H-2') ppm.

$C_{12}H_{11}NOS$: 217 g/mol

8.5.1.15 *t*-Butyl(phenyl)sulfide (69)[71]



To a 25 ml flask containing glacial acetic acid (7.5 ml), 70% $HClO_4$ (1.6 ml) was added, followed by acetic acid anhydride (1.3 ml). The stirred solution was cooled in an ice bath and thiophenol (5.00 mmol, 551 mg, 511 µl) was added with stirring. This was followed by the addition of *t*-butanol (10.0 mmol, 741 mg, 956 µl). The reaction mixture was stirred overnight. Water (20 ml) and diethyl ether (20 ml) were added to the mixture and the layers were separated. The aqueous layer was extracted with diethyl ether (2 x 15 ml). First the combined organic layers were washed with 20% aqueous sodium hydroxide solution (2 x 20 ml) until alkaline and then additionally washed with water (3 x 20 ml) until neutral. The organic layers were dried (Na_2SO_4), then filtrated and the solvent was

removed under reduced pressure. The crude colourless liquid was obtained in 97% yield (805 mg, 4.85 mmol) and used without further purification. The obtained spectroscopic data are in agreement with literature data.

R_f (EA/Hex 1:1) = 0.63.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53–7.56 (m, 2H), 7.31–7.37 (m, 3H), 1.29 (s, 9H, $C(CH_3)_3$) ppm.

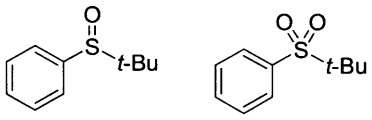
^{13}C NMR (62 MHz, $CDCl_3$): δ = 137.4, 132.8, 128.6, 128.4, 45.7 ($C(CH_3)_3$), 31.0 ($C(CH_3)_3$) ppm.

MS (AP+) m/z (%): 184 ($[M+NH_4]^+$, 100), 125 (10).

IR (film): $\tilde{\nu}$ = 3073, 2961, 2898, 2861, 1582, 1473, 1455, 1437, 1390, 1363, 1304, 1168, 1091, 1066, 1025, 750, 694 cm^{-1}.

$C_{10}H_{14}S$: 166 g/mol.

8.5.1.16 *rac*-1-(*t*-Butylsulfinyl)benzene (*rac*-70)[138] and 1-(*t*-butylsulfonyl)benzene (85)[139]



To a solution of sodium(meta)periodate (20.2 mmol, 4,33 g) in distilled water (75 ml), *t*-butyl(phenyl)sulfane (15.0 mmol, 2.49 g) in THF (15 ml) was added at 0 °C. The mixture was stirred in an open flask over night whereas the temperature rose to room temperature. Then dichloromethane (50 ml) was added and the layers separated. The aqueous layer was washed with dichloromethane (3 x 30 ml) and the combined organic layers were stirred with activated carbon and dried with Na_2SO_4. After filtration, the solvent was removed under reduced pressure. The two products were separated by silica gel column chromatography (hexane/ethyl acetate 1:4→1:1). The obtained spectroscopic data are in good agreement with literature data.

***rac*-1-(*t*-Butylsulfinyl)benzene 70** was obtained with 51% yield (1.39 g, 7.65 mmol) as a colourless solid.

R_f (EA/Hex 1:1) = 0.31.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.57–7.61 (m, 2H), 7.47–7.51 (m, 3H), 1.17 (s, 9H, $C(CH_3)_3$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.0 (*C*-1), 131.1 (*C*-4), 128.3, 126.3, 55.8 ($C(CH_3)_3$), 22.8 ($C(CH_3)_3$) ppm.

MS (ES+) m/z (%): 182 ($[M+H]^+$, 22), 126 (100), 110 (34), 97 (83), 78 (99).

IR (KBr): $\tilde{\nu}$ = 3059, 2975, 1736, 1444, 1363, 1286, 1133, 1079, 1039, 941, 751, 726, 691, 641 cm^{-1}.

$C_{10}H_{14}SO$: 182 g/mol.

1-(*t*-Butylsulfonyl)benzene was obtained with 21% yield (624 mg, 3.15 mmol) as a colourless solid.

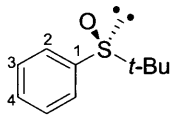
R_f (EA/Hex 1:3) = 0.45.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 7.3 Hz, 2H, C*H*-2), 7.68 (m, 1H, C*H*-4), 7.58 (t, *J* = 7.3 Hz, 2H, C*H*-3), 1.37 (s, 9H, $C(CH_3)_3$) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.4 (*C*-1), 133.5(*C*-4), 130.5, 128.7, 59.8 ($C(CH_3)_3$), 23.6 ($C(CH_3)_3$) ppm.

$C_{10}H_{14}SO$: 198 g/mol.

8.5.1.17 (-)-(*S*)-*t*-Butylphenyl sulfoxide [(*S*)-70][58]



To a solution of 2,2-diphenyl-1,2-dihydroxy-propyl-2-*O*-*t*-butylsulfinate (0.600 mmol, 200 mg) in 4 ml dry THF, PhMgBr (3 M solution in diethylether, 1.32 mmol, 0.44 ml) was added slowly at room temperature. The mixture was stirred for 1 hour and then quenched with water (4 ml). The aqueous mixture was extracted with ethyl acetate (2 x 5 ml) and the combined organic layers were washed with water (10 ml), and then dried with $MgSO_4$. The solvent was removed in vacuo. After column chromatography (hexane/ethyl acetate 3:1) the product was isolated with 46% yield (50 mg, 0.28 mmol) as a colourless oil. The obtained spectroscopic data are in agreement with literature data.

R_f (EA/Hex 1:3) = 0.12.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.54 (m, 2H, Ar*H*), 7.40–7.43 (m, 3H, Ar*H*), 1.10 (s, 9H, $C(CH_3)_3$) ppm.

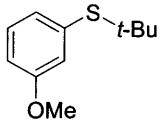
^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.0 (*C*-1), 131.1 (*C*-4), 128.3, 126.3, 55.7 ($C(CH_3)_3$), 22.8 ($C(CH_3)_3$) ppm.

HPLC: Column: *Chiracel® OD-H*; Solvents: hexane/i-propanol 95:5; Flow rate: 0.5 ml/min; Temperature: 10 °C; Detector: 217 nm; t_R: 10.37 min, t_R: 12.18 min.

[α] $_D^{20}$ = –188 (c = 0.1, CH_2Cl_2).

$C_{10}H_{14}SO$: 182 g/mol.

8.5.1.18 *t*-Butyl-(3-methoxyphenyl) sulfone (73)[140]



To a 25 ml flask containing glacial acetic acid (23 ml), 70% $HClO_4$ (5 ml) was added, followed by acetic acid anhydride (4 ml). The stirred solution was cooled in an ice bath and 3-methoxythiophenol (14.5 mmol, 1.80 ml) was added with stirring. This was followed by the addition of *t*-butanol (29.0 mmol, 2.80 ml). The reaction mixture was stirred overnight. Water (50 ml) and diethyl ether (50 ml) were added to the mixture and the phases were separated. The aqueous layer was extracted with diethyl ether (2 x 50 ml). First the combined organic layers were washed with 20% aqueous sodium hydroxide solution (2 x 100 ml) until alkaline and then additionally washed with water (3 x 100 ml) until neutral. The organic layers were dried (Na_2SO_4), then filtrated and the solvent was removed under reduced pressure. The crude colourless liquid was obtained in 98% yield (346 mg, 1.76 mmol) and used without further purification. The obtained spectroscopic data are in agreement with literature data.

R_f (EA/Hex 1:3) = 0.65.

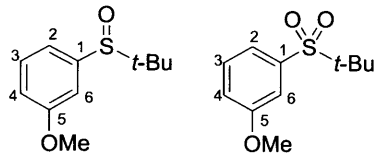
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22–7.26 (m, 1H, Ar*H*), 7.08–7.14 (m, 2H, Ar*H*), 6.91 (ddd, *J* = 0.9 Hz, *J* = 2.6 Hz, *J* = 8.2 Hz, 1H, C*H*-3), 3.81 (s, 3H, OCH_3), 1.30 (s, 9H, (C(CH_3)$_3$)) ppm.

IR (film): $\tilde{\nu}$ = 2997, 2958, 2865, 2834, 1590, 1575, 1554, 1481, 1394, 1386, 1362, 1282, 1230, 1182, 1166, 1142, 1078, 1037, 883, 862, 827, 776, 693, 686 cm^{-1}.

MS (CI+) m/z (%): 197 ([M+H]$^+$, 100), 140 (6), 53 (3).

$C_{11}H_{16}SO$: 196 g/mol.

8.5.1.19 *rac*-1-(*t*-Butylsulfinyl)-3-methoxybenzene (*rac*-74) and 1-(*t*-butylsulfonyl)-3-methoxybenzene (86)



To a solution of sodium(meta)periodate (19.0 mmol, 4.06 g) in water (75 ml), *t*-butyl-(3-methoxyphenyl)sulfane (14.2 mmol, 2.77 g) in THF (15 ml) was added at 0 °C. The mixture was stirred in an open flask over night whereas the temperature rose to room temperature. Then dichloromethane (50 ml) was added and the layers separated. The aqueous layer was washed with dichloromethane (3 x 50 ml) and the combined organic layers were stirred with activated carbon, dried with Na_2SO_4. After filtration, the solvent was removed under reduced pressure. The two products were separated by silica gel column chromatography (hexane/ethyl acetate 1:4→1:3).

1-(*t*-Butylsulfinyl)-3-methoxybenzene (74) was obtained with 54% yield (1.63g, 7.67 mmol) as a colourless solid.

R_f (EA/Hex 1:3) = 0.25.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (t, *J* = 8.1 Hz, 1H, C*H*-3), 7.17 (dd, *J* = 1.6 Hz, *J* = 2.5 Hz, 1H, C*H*-6), 7.09 (m, 1H, C*H*-2), 7.01 (ddd, *J* = 0.7 Hz, *J* = 2.5 Hz, *J* = 8.1 Hz, 1H, C*H*-4), 3.84 (s, 3H, OCH_3), 1.17 (s, 9H, (C(CH_3)$_3$),) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.8 (*C*), 141.3 (*C*), 129.2 (*C*H), 118.7 (*C*H), 117.5 (*C*H), 110.7 (*C*H), 56.0, 55.6, 22.9 (C(*C*H$_3$)$_3$) ppm.

IR (neat): $\tilde{\nu}$ = 2962, 1594, 1578, 1474, 1427, 1364, 1319, 1284, 1234, 1172, 1089, 1070, 1040, 991, 871, 786, 691 cm^{-1}.

MS (ES+) m/z (%): 447 (63), 425 ([2M+H]$^+$, 100), 213 ([M+H]$^+$, 80), 157 (48), 139 (12).

HRMS (ES+): [M+H]$^+$ calculated for $C_{11}H_{17}SO_2$: 213.0944, found: 213.0943.

M.P.: 78–79 °C.

$C_{11}H_{16}O_3S$: 212 g/mol.

1-(*t*-Butylsulfonyl)-3-methoxybenzene (86) was obtained in 35% yield (1.13 g, 4,97 mmol) as a colourless solid.

R_f (EA/Hex 1:3) = 0.50.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.43 (m, 2H), 7.31–7.34 (m, 1H), 7.10–7.16 (m, 1H), 3.82 (s, 3H, OCH_3), 1.31 (s, 9H, (C(CH_3)$_3$)) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.6 (*C*), 136.5 (*C*), 129.7 (*C*H), 122.7 (*C*H), 119.8 (*C*H), 115.1 (*C*H), 60.0, 55.7, 22.9 (C(*C*H$_3$)$_3$) ppm.

IR (neat): $\tilde{\nu}$ = 3085, 3068, 2980, 2967, 2945, 2844, 1598, 1580, 1479, 1427, 1397, 1364, 1316, 1291, 1246, 1192, 1127, 1047, 1043, 911, 900, 854, 796, 705, 653 cm^{-1}.

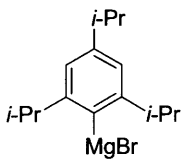
MS (ES+) *m/z* (%): 479 (27), 246 ([M+NH_4]$^+$, 100), 229 ([M+H]$^+$, 9), 173 (17).

HRMS (ES+): [M+NH_4]$^+$ calculated for $C_{11}H_{20}SO_3N$ 246.1158, found: 246.1159.

M.P.: 74–75 °C.

$C_{11}H_{16}O_3S$: 228 g/mol.

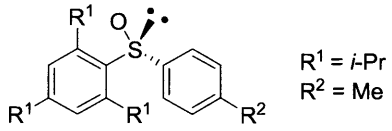
8.5.1.20 (2,4,6-Triisopropylphenyl)magnesium bromide (76)



A two-neck round-bottom flask containing magnesium (27.5 mmol, 668.3 mg) was equipped with a reflux condenser, and 3 ml dry THF were added. 2,4,6-Triisopropylphenyl bromide (7.1 mmol, 2.0 g) was added dropwise until the reaction mixture started to reflux. After 5 min 2 drops 1,2-

dibromoethane were added if no reaction occurred. Once the reaction began to reflux, further 2,4,6-triisopropylphenyl bromide (17.9 mmol, 5.1 g) and dry THF (7 ml) were added slowly. After the addition was complete, the mixture was refluxed for 12 h. The Grignard reagent was used without further purification.

8.5.1.21 (*R*)-4-Methyl-1-[(2,4,6-triisopropylphenyl)sulfinyl]benzene (77)



To a solution of (–)-(1*R*,2*S*,5*R*)-menthyl-(*S*)-4-toluenesulfinate (1.00 mmol, 294 mg) in 5 ml dry THF, freshly prepared (2,4,6-triisopropylphenyl)magnesium bromide (1.5 mmol) was slowly added at 0 °C. The mixture was stirred at 0 °C for 3 h, quenched with water (5 ml) and extracted with diethyl ether (3 x 10 ml). The combined organic phases were dried with Na_2SO_4, filtrated and the solvent was removed under reduced pressure. After column chromatography (petroleum ether/diethyl ether, 10:1) the product was isolated with 60% yield (205 mg, 0.60 mmol) as colourless solid.

R_f (E/PE 1:10) = 0.58.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.18–7.23 (m, 2H, Ar*H*), 7.13–7.19 (m, 2H, Ar*H*), 7.01 (s, 2H, Ar*H*), 3.65–3.71 (m, 2H, C*H*$(CH_3)_2$), 2.78–2.82 (m, 1H, C*H*$(CH_3)_2$), 2.29 (s, 3H, ArCH_3), 1.19 (m, 18H, CH(CH_3)$_2$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.2, 151.2, 143.2, 139.3, 135.7, 129.5, 124.6, 123.4, 34.4, 24.7, 23.7 ppm.

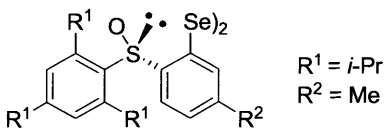
IR (KBr): $\tilde{\nu}$ = 2956, 1598, 1560, 1492, 1458, 1423, 1382, 1362, 1301, 1083, 1042, 1025, 809 cm^{-1}.

MS (ES+): m/z (%): 343 ([M+H]$^+$, 100), 327 (83), 312 (3), 285.3 (2), 250 (3), 233 (5), 189 (8), 161 (5), 140 (18), 124 (10), 108 (15), 98 (6), 91 (10), 84 (10), 72 (10), 58 (10), 44 (10).

HRMS (ES+): [M+H]$^+$ calculated for $C_{22}H_{30}OS$: 343.2090; found 343.2091.

$C_{22}H_{30}OS$: 342 g/mol.

8.5.1.22 (*R*,*R*)-Bis{5-methyl-2-[(2,4,6-triisopropylphenyl)sulfinyl]phenyl} diselenide (78)



To a solution of diisopropylamine (2.58 mmol, 362 µl) in dry THF (8 ml) under argon, *n*-butyllithium (2.40 mmol, 960 µl, 2.5 M solution in hexane) was added at 0 °C. After 15 min the solution was cooled to –78 °C and (*R*)-4-methyl-1-[(2,4,6-triisopropylphenyl)sulfinyl] benzene (0.860 mmol, 292

mg) in dry THF (3 ml) was added. This mixture was stirred at –78 °C for 90 min and then warmed to 0 °C. After 10 min selenium (209 mg, 2.65 mmol) was added with vigorous stirring and the mixture was warmed to room temperature with stirring overnight. To this mixture, 1 M HCl (15 ml) was added and the layers were separated. The aqueous layer was washed with diethyl ether (3 x 10 ml) and the combined organic layers were stirred with potassium hydroxide (100 mg) and dried with Na_2SO_4. After filtration, the solvent was removed under reduced pressure and column chromatography (petroleum ether/diethyl ether, 2:1) afforded the diselenide in 6% yield (43 mg, 0.15 mmol) as yellow oil.

R_f (EA/Hex 1:3) = 0.55.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (br. s, 2H, Ar*H*), 7.14 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.02 (m, 6H, Ar*H*), 3.69–3.76 (m, 4H, C*H*$(CH_3)_2$), 2.83 (sept, *J* = 7.0 Hz, 2H, C*H*$(CH_3)_2$], 2.27 (s, 6H, ArCH_3), 1.18 (d, *J* = 7.0 Hz, 12H, CH(CH_3)$_2$), 1.13 (d, *J* = 7.0 Hz, 24H, CH(CH_3)$_2$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.8, 151.5, 142.7, 141.2, 134.8, 134.5, 129.9, 128.3, 126.1, 123.3, 34.4, 29.2, 24.1, 23.7, 21.1 ppm.

IR (film): $\tilde{\nu}$ = 2961, 2926, 2868, 1595, 1456, 1384, 1363, 1045, 1018, 909, 732 cm^{-1}.

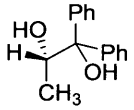
^{77}Se NMR (57 MHz, $CDCl_3$): δ = 452 ppm.

MS (NES+): m/z (%): 921 (8), 843 ([M+H]$^+$, 100), 523 (5), 391 (4).

HRMS (NES+): [M+H]$^+$ calculated for $C_{44}H_{59}O_2S_2{}^{76}Se_2$: 835.2335; found 835.2336.

$C_{44}H_{58}O_2S_2Se_2$: 841 g/mol.

8.5.1.23 (*S*)-1,1-Diphenylpropane-1,2-diol (81)[59]



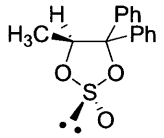
To a solution of *L*-(–)-ethyl lactate (2.00 mmol, 236 mg, 229 µl) in 20 ml dry THF, phenylmagnesium bromide (3 M in diethylether, 6.0 mmol, 2.0 ml) was slowly added at 0 °C under an argon atmosphere. The mixture was stirred for 18 h at 0 °C, then quenched with saturated NH_4Cl-solution (10 ml) and the layers were separated. The aqueous layer was extracted with diethyl ether (3 x 10 ml) and the combined organic extracts were dried with Na_2SO_4. After the solvent was removed under reduced pressure and column chromatography (petroleum ether/diethyl ether 10:1), the product was obtained as colourless oil in 77% yield (350 mg, 1.54 mmol). The obtained spectroscopic data are in agreement with literature data.

R_f (EA/Hex 1:3) = 0.20.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (dd, *J* = 1.0 Hz, *J* = 8.0 Hz, 2H, Ar*H*), 7.32 (dd, *J* = 1.0 Hz, *J* = 8.0 Hz, 2H, Ar*H*), 7.23 (td, *J* = 1.0 Hz, *J* = 8.0 Hz, 2H, Ar*H*), 7.20–7.05 (m, 4H, Ar*H*), 4.65 (q, *J* = 6.0 Hz, 1H, C*H*CH_3), 3.08 (s, br, 1H, O*H*), 2.01 (s, br, 1H, O*H*), 0.96 (d, *J* = 6.0 Hz, 3H, CHC*H*$_3$) ppm.

$C_{15}H_{16}O_2$: 228 g/mol.

8.5.1.24 (–)-(2*R*, 5*S*)-*trans*-4,4-Diphenyl-5-methyl-1,3,2-dioxathiolane-2-oxide [(S_S)-82][59]



To a solution of (*S*)-1,1-diphenylpropane-1,2-diol (1.54 mmol, 350 mg) in dry dichloromethane (2.5 ml), a solution of $SOCl_2$ (2.31 mmol, 168 µl) in dichloromethane (0.8 ml) was added at one time at –40 °C. The flask was maintained at this temperature and then triethylamine (3.85 mmol, 390 mg, 534 µl) in dichloromethane (4.5 ml) was added dropwise. A white precipitate appeared and the reaction was quenched with water (3 ml). The aqueous phase was extracted with dichloromethane (3 x 5 ml) and the combined organic layers were dried with $MgSO_4$, filtrated and evaporated. The crude solid product (dr: 3.5/1 according to crude NMR) was crystallised in diethylether/hexane to afford pure (–)-(2*R*,5*S*)-*trans*-4,4-diphenyl-5-methyl-1,3,2-dioxathiolane-2-oxide as colourless solid in 60% yield (253 mg, 0.924 mmol). The obtained spectroscopic data are in agreement with literature data.

R_f (E/PE 1:1) = 0.66.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.36 (m, 3H, Ar*H*), 7.31–7.33 (m, 2H, Ar*H*), 7.22–7.26 (m, 3H, Ar*H*), 6.93–6.97 (m, 2H, Ar*H*), 5.64 (q, *J* = 6.0 Hz, 1H, C*H*CH_3), 1.22 (d, *J* = 6.0 Hz, 3H, CHC*H*$_3$) ppm.

MS (ES+) m/z (%): 292 ($[M+NH_4]^+$, 100), 228 (4), 211 (55), 133 (3).

HRMS (ES+): $[M+NH_4]^+$ calculated for $C_{15}H_{18}NO_3S$: 292.1002, found: 292.1005.

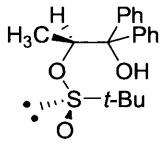
$C_{15}H_{14}O_3S$: 274 g/mol.

The epimer (*R*$_S$)-**83** was enriched in the mother liquor of the above recrystallisation, but not further purified.

R_f (E/PE 1:1) = 0.60.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.36 (m, 3H, Ar*H*), 7.31–7.33 (m, 2H, Ar*H*), 7.22–7.26 (m, 3H, Ar*H*), 6.93–6.97 (m, 2H, Ar*H*), 5.49 (q, *J* = 6.0 Hz, 1H, C*H*CH_3), 1.27 (d, *J* = 6.0 Hz, 3H, CHC*H*$_3$) ppm.

8.5.1.25 2,2-Diphenyl-1,2-dihydroxypropyl-2-*O*-*t*-butylsulfinate (83)[59]



To a solution of (–)-(2*R*,5*S*)-*trans*-4,4-diphenyl-5-methyl-1,3,2-dioxathiolane-2-oxide (7.4 mmol, 2.0 g) in dry THF (75 ml), *t*-BuMgCl (2 M solution in diethylether, 7.50 mmol, 3.75 ml) was added slowly at –78 °C. The mixture was stirred overnight and the temperature was allowed to rise to –50 °C during this time. The mixture was quenched with 50 ml water and extracted with diethyl ether (3 x 50 ml). The combined organic phases were dried with $MgSO_4$ and the solvent was removed under reduced pressure. After column chromatography (hexane/ethyl acetate 4:1) the title compound was isolated with 56% yield (1.36 g, 4.14 mmol) as colourless oil. The obtained spectroscopic data are in agreement with literature data.

$\mathbf{R_f}$ (EA/Hex 1:3) = 0.15.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.40 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.25–7.18 (m, 4H, Ar*H*), 7.12–7.08 (m, 2H, Ar*H*), 5.29 (m, 1H, C*H*CH_3), 3.08 (s, 1H, O*H*), 1.30 (d, *J* = 6.0 Hz, 3H, CHC*H*$_3$), 0.80 (s, 9H, C(C*H*$_3$)$_3$) ppm.

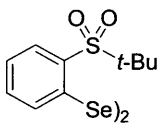
^{13}C NMR (63 MHz, $CDCl_3$): δ = 145.2 (*C*), 143.2 (*C*), 128.3 (*C*H), 128.3 (*C*H), 127.1 (*C*H), 127.0 (*C*H), 126.2 (*C*H), 125.6 (*C*H), 82.5, 79.7, 57.8 (*C*(CH$_3$)$_3$), 21.5 (C(*C*H$_3$)$_3$), 16.3 (CH*C*H$_3$) ppm.

$C_{19}H_{24}O_3S$: 332 g/mol.

8.5.1.26 For 1-(*t*-butylsulfonyl)benzene (85)[139] see 8.5.1.16

8.5.1.27 For 1-(*t*-butylsulfonyl)-3-methoxybenzene (86) see 8.5.1.19

8.5.1.28 Bis[2-(*t*-butylsulfonyl)phenyl] diselenide (87)



Synthesised according to GP 2 with 505 mg (2.55 mmol) 1-(*t*-butylsulfonyl)benzene, *n*-butyllithium (2.80 mmol, 1.12 ml, 2.5 M solution in hexanes) and selenium (221 mg, 2.80 mmol). After column chromatography (hexane/ethylacetate 4:1→1:4), the diselenide was isolated with 28% yield (394 mg, 0.714 mmol) as yellow oil which crystallized from diethyl ether upon standing.

R_f (EA/Hex 2:1) = 0.20.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.76 (ddd, *J* = 1.7 Hz, *J* = 7.5 Hz, *J* = 18.5 Hz, 4H, Ar*H*), 7.33 (dt, *J* = 1.7 Hz, *J* = 7.5 Hz, *J* = 18.5 Hz, 4H, Ar*H*), 1.38 (s, 18H, C(C*H*$_3$)$_3$) ppm.

^{13}C NMR (126 MHz, $CDCl_3$): δ = 134.3 (*C*H), 133.9 (*C*), 133.7 (*C*H), 132.9 (*C*), 131.6 (*C*H), 126.8 (*C*H), 62.6 (*C*(CH$_3$)$_3$), 23.8 (C(*C*H$_3$)$_3$) ppm.

^{77}Se NMR (57 MHz, $CDCl_3$): δ = 477 ppm.

IR (film): $\tilde{\nu}$ = 2985, 1573, 1559, 1476, 1440, 1421, 1395, 1364, 1293, 1278, 1252, 1193, 1139, 1114, 1086, 1039, 1021, 799, 761, 736, 707, 649, 634, 570 cm^{-1}.

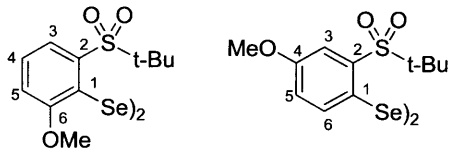
MS (ES+): m/z (%): 1024 ([2M+NH$_4$]$^+$, 35), 572 ([M+NH$_4$]$^+$, 100), 481 (6), 216 (8).

HRMS: (ES+): [M+NH$_4$]$^+$ calculated for $C_{20}H_{30}O_4S_2{}^{74}Se^{76}SeN$: 562.0028; found 562.0032.

M.P.: 204–206 °C (crystals from diethyl ether).

$C_{20}H_{26}S_2O_4Se_2$: 552 g/mol.

8.5.1.29 Bis[2-(*t*-butylsulfonyl)-6-methoxyphenyl] diselenide (88) and bis[2-(*t*-butylsulfonyl)-4-methoxyphenyl] diselenide (89)



Synthesised according to GP 2 with 2.0 g (8.8 mmol) 1-(*t*-butylsulfonyl)-3-methoxybenzene, *n*-butyllithium (9.60 mmol, 3.84 ml, 2.5 M solution in hexanes) and selenium (758 mg, 9.60 mmol). After column chromatography (hexane/ethyl acetate, 1:1→0:1) the products were isolated as yellow amorphous solids which were crystallised from chloroform.

Bis[2-(*t*-butylsulfonyl)-6-methoxyphenyl] diselenide (88): Yield: 3% (162 mg, 0.264 mmol); yellow crystals.

R_f (EA) = 0.20.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52 (dd, *J* = 1.0 Hz, *J* = 7.9 Hz, 2H, Ar*H*), 7.38 (t, *J* = 8.1 Hz, 2H, C*H*-4), 7.10 (dd, *J* = 1.0 Hz, *J* = 8.1 Hz, 2H, Ar*H*), 3.92 (s, 6H, OC*H*$_3$), 1.19 (s, 18H, C(C*H*$_3$)$_3$) ppm.

^{13}C NMR (500 MHz, $CDCl_3$): δ = 160.4 (*C*-6), 139.1 (*C*-2), 128.8 (*C*H), 125.4 (*C*H), 124.0 (*C*-1), 115.6 (*C*H), 61.4, 56.8, 24.0 (C(*C*H$_3$)$_3$) ppm.

^{77}Se NMR (57 MHz, $CDCl_3$): δ = 465 ppm.

IR (film): $\tilde{\nu}$ = 2972, 2926, 1570, 1458, 1432, 1286, 1260, 1183, 1156, 1106, 1029, 841, 790, 723, 656 cm^{-1}.

MS (ES+): m/z (%): 614 ($[M+H]^+$, 80), 556 (10), 534 (10), 438 (8), 372 (3), 356 (7), 292 (13), 251 (100), 234 (55), 186 (25), 172 (10), 57 (65).

HRMS (ES+): $[M+H]^+$ calculated for $C_{22}H_{30}O_6S_2{}^{76}Se_2$: 605.9863; found 605.9866.

M.P. (crystals from $CHCl_3$): 253–256 °C.

$C_{22}H_{30}S_2O_6Se_2$: 613 g/mol.

Bis[2-(*t*-butylsulfonyl)-4-methoxyphenyl] diselenide (89): Yield: 8% (431 mg, 0.704 mmol); yellow crystals.

R_f (EA) = 0.47.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.9 Hz, 2H, Ar*H*), 7.38 (d, *J* = 2.8 Hz, 2H, Ar*H*), 6.99 (dd, *J* = 2.9 Hz, *J* = 8.9 Hz, 2H, Ar*H*), 3.82 (s, 6H, OCH_3), 1.45 (s, 18H, C(CH_3)$_3$) ppm.

^{13}C NMR (500 MHz, $CDCl_3$): δ = 159.0 (*C*-4), 134.5 (*C*-2), 133.3 (*C*H), 123.0 (C-1), 121.2 (*C*H), 118.8 (*C*H), 63.1, 56.3, 24.3 (C(*C*H_3)$_3$) ppm.

^{77}Se NMR (57 MHz, $CDCl_3$): δ = 467 ppm.

IR (film): $\tilde{\nu}$ = 2971, 1591, 1465, 1435, 1291, 1259, 1230, 1145, 1037, 707, 653 cm^{-1}.

MS (ES+): m/z (%): 614 ($[M+H]^+$, 80), 556 (15), 438 (12), 372 (5), 308 (10), 292 (17), 251 (100), 234 (60), 186 (30), 171 (11), 77 (6), 57 (81).

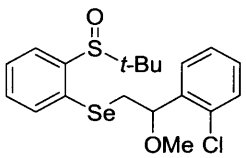
HRMS (ES+): $[M+H]^+$ calculated for $C_{22}H_{30}O_6S_2{}^{76}Se_2$: 605.9863; found 605.9866.

M.P. (foam): 85 °C. **M.P.** (crystals from $CHCl_3$): 193–196 °C.

$C_{22}H_{30}S_2O_6Se_2$: 613 g/mol.

8.5.2 Selenium Electrophiles

8.5.2.1 *rac*-*t*-Butyl[2-{(2-methoxy-2-(2-chloro)phenyl)ethyl]seleno}phenyl]sulfoxide (101)



Synthesised according to GP 3 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 38 µl

2-chlorostyrene (0.30 mmol, 42 mg) in dichloromethane with 100 µl dry methanol. After column chromatography (hexane/ethyl acetate, 5:1→1:1) the product was isolated as a mixture of diastereomers (*d.r.*: 11:1) in 41% yield (35 mg, 0.082 mmol) as colourless oil.

R_f (EA/Hex 1:3) = 0.17.

MS (ES+) m/z (%): 861 (5), 431 ($[M+H]^+$, 100), 342 (23), 204 (14).

HRMS (ES+): $[M+H]^+$ calculated for $C_{19}H_{24}O_2{}^{35}ClS^{74}Se$: 425.0405; found 425.0410.

IR (film): $\tilde{\nu}$ = 3055, 2929, 2824, 1571, 1471, 1444, 1360, 1227, 1167, 1105, 1047, 1022, 965, 757, 705 cm^{-1}.

Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (dd, *J* = 1.5 Hz, *J* = 7.7 Hz, 1H, Ar*H*), 7.57 (dd, *J* = 1.0Hz, *J* = 7.7 Hz, 1H, Ar*H*), 7.35–7.46 (m, 2H, Ar*H*), 7.22–7.33 (m, 2H, Ar*H*) 7.17 (d, *J* = 1.5 Hz, 1H, Ar*H*), 7.15 (d, *J* = 1.5 Hz, 1H, Ar*H*), 4.83 (dd, *J* = 3.8 Hz, *J* = 8.5 Hz, 1H, C*H*OCH$_3$), 3.24 (s, 3H, OC*H*$_3$), 3.10–3.23 (m, 2H, SeC*H*$_2$CH), 1.19 (s, 9H, C(C*H*$_3$)$_3$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.5 (*C*), 138.1 (*C*), 134.1 (*C*H), 132.8 (*C*), 131.7 (*C*), 131.3 (*C*H), 129.5 (*C*H), 129.0 (*C*H), 127.4 (*C*H), 127.4 (*C*H), 127.3 (*C*H), 127.1 (*C*H), 79.3 (*C*HOCH$_3$), 58.2 (*C*(CH$_3$)$_3$), 57.4 (O*C*H$_3$), 35.6 (Se*C*H$_2$CH), 23.3 (C(*C*H$_3$)$_3$) ppm.

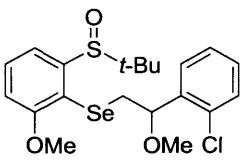
Minor isomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (dd, *J* = 1.4 Hz, *J* = 7.9 Hz, 1H, Ar*H*), 7.53 (dd, *J* = 1.0 Hz, *J* = 7.9 Hz, 1H, Ar*H*), 7.35–7.46 (m, 2H, Ar*H*), 7.22–7.33 (m, 2H, Ar*H*), 7.19 (d, *J* = 3.8 Hz, 1H, Ar*H*), 7.13 (d, *J* = 1.7 Hz, 1H, Ar*H*), 4.68 (dd, *J* = 3.3 Hz, *J* = 9.3 Hz, 1H, C*H*OCH$_3$), 3.24 (s, 3H, OC*H*$_3$), 3.10–3.23 (m, 1H, SeC*H*HCH), 3.02 (dd, *J* = 9.3 Hz, *J* = 12.4 Hz, 1H, SeCH*H*CH), 1.19 (s, 9H, C(C*H*$_3$)$_3$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.7 (*C*), 138.1 (*C*), 134.1 (*C*H), 132.9 (*C*), 131.6 (*C*), 131.3 (*C*H), 129.6 (*C*H), 129.0 (*C*H), 127.4 (*C*H), 127.4 (*C*H), 127.2 (*C*H), 127.1 (*C*H), 78.8 (*C*HOCH$_3$), 58.1 (*C*(CH$_3$)$_3$), 57.6 (O*C*H$_3$), 35.8 (Se*C*H$_2$CH), 23.3 (C(*C*H$_3$)$_3$) ppm.

$C_{19}H_{23}ClSO_2Se$: 430 g/mol.

8.5.2.2 *rac*-2-(*t*-Butylsulfinyl)-6-methoxyphenyl 2-(2-chlorophenyl)-2-methoxyethyl selenide (102)



Synthesised according to GP 3 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)-6-methoxyphenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 38 µl

2-chlorostyrene (0.30 mmol, 42 mg) in chloroform at –50 °C with 100 µl dry methanol. After column chromatography (hexane/ethyl acetate, 5:1→1:1) the product was isolated as a mixture of diastereomers (*d.r.*: 2:1) in 40% yield (37 mg, 0.08 mmol) as colourless oil.

R_f (E) = 0.17.

MS (ES+) m/z (%) = 524 ([M+MeCNNa]$^+$, 100), 483 ([M + Na]$^+$, 68).

HRMS (ES+): [M+H]$^+$ calculated $C_{20}H_{26}O_3{}^{35}ClS^{80}Se$ 461.0456, found 461.0468.

IR (film): $\tilde{\nu}$ = 2934, 1568, 1455, 1428, 1361, 1285, 1260, 1169, 1149, 1104, 1040, 1026, 834, 786, 759, 732, 706 cm^{-1}.

Major isomer:

^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.40 (m, 3H, Ar*H*), 7.22 (m, 1H, Ar*H*), 7.18 (m, 1H, Ar*H*), 7.10 (m, 1H, Ar*H*) 6.87 (m, 1H, Ar*H*), 4.88 (dd, *J* = 3.5 Hz, *J* = 9.1 Hz, 1H, C*H*OCH$_3$), 3.86 (s, 3H, OC*H*$_3$), 3.20 (m, 4H, OC*H*$_3$ and SeC*H*HCH), 2.96 (dd, *J* = 3.5 Hz, *J* = 12.2 Hz, 2H, SeCH*H*CH), 1.15 (s, 9H, C(C*H*$_3$)$_3$) ppm.

^{13}C NMR (63 MHz, $CDCl_3$): δ = 159.2 (*C*), 146.8 (*C*), 138.2 (*C*), 132.7 (*C*), 129.5 (*C*H), 129.3 (*C*H), 128.9 (*C*H), 127.4 (*C*H), 127.2 (*C*H), 119.6 (2*C*H), 112.5 (*C*H), 79.9 (*C*OCH$_3$), 58.3 (*C*(CH$_3$)$_3$), 57.5 (O*C*H$_3$), 56.3 (O*C*H$_3$), 34.3 (ArSe*C*H$_2$), 23.6 (C(*C*H$_3$)$_3$) ppm.

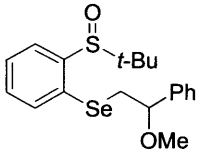
Minor Isomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.38 (dd, *J* = 1.7 Hz, *J* = 8.0 Hz, 1H, Ar*H*), 7.23 (m, 3H, Ar*H*), 7.13 (m, 1H, Ar*H*), 6.85 (dd, *J* = 2.9 Hz, *J* = 8.5 Hz, 1H, Ar*H*), 4.76 (dd, *J* = 3.6 Hz, *J* = 8.8 Hz, 1H, C*H*OCH$_3$), 3.78 (s, 3H, OC*H*$_3$), 3.22 (s, 3H, OC*H*$_3$), 3.07 (dd, *J* = 8.8 Hz, *J* = 12.5 Hz, 1H, SeC*H*HCH), 2.99 (dd, *J* = 3.6 Hz, *J* = 12.5 Hz, 1H, SeCH*H*CH), 1.17 (s, 9H, C(C*H*$_3$)$_3$] ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.9 (*C*), 146.8 (*C*), 138.0 (*C*), 137.3 (*C*), 132.9 (*C*H), 129.6 (*C*H), 128.0 (*C*H), 127.3 (*C*H), 127.1 (*C*H), 118.8 (2x*C*H), 111.6 (*C*H), 79.4 (*C*OCH$_3$), 58.5 (*C*(CH$_3$)$_3$), 57.4 (O*C*H$_3$), 55.7 (O*C*H$_3$), 36.2 (ArSe*C*H$_2$), 23.5 (C(*C*H$_3$)$_3$) ppm.

$C_{20}H_{25}ClSO_3Se$: 460 g/mol.

8.5.2.3 *rac-t*-Butyl[2-{(2-methoxy-2-phenyl)ethyl]seleno}phenyl]sulfoxide (103)



Synthesised according to GP 3 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 34 µl styrene (0.30 mmol, 31 mg) in tetrahydrofuran with 100 µl dry methanol. After column chromatography (hexane/ethyl acetate, 5:1→1:1) the product was isolated as a mixture of diastereomers (*d.r.*: 5:1) in 52% yield (41 mg, 0.082 mmol) as pale yellow oil.

R_f (EA/Hex 1:3) = 0.20.

IR (film): $\tilde{\nu}$ = 3056, 2934, 1643, 1570, 1443, 1267, 1151, 1102, 1030, 958, 851, 738, 703, 640, 591 cm^{-1}.

MS (ES+) m/z (%): 815 (20), 793 ($[2M+H]^+$, 25), 752 (3), 664 (5), 455 (13), 419 (19), 397 ($[M+H]^+$, 100), 309 (14), 261 (10), 216 (18).

HRMS (ES+) $[M+H]^+$: calculated for $C_{19}H_{25}O_2S^{74}Se$: 391.0795; found 391.0800.

Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 1.4 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.48 (dd, *J* = 1.0 Hz, *J* = 7.6 Hz, 1H, Ar*H*), 7.36 (ddd, *J* = 1.3 Hz, *J* = 7.6 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.23–7.29 (m, 6H, Ar*H*), 4.28 (dd, *J* = 5.0 Hz, *J* = 8.3 Hz, 1H, C*H*OCH$_3$), 3.29 (dd, *J* = 8.3 Hz, *J* = 12.1 Hz, 1H, SeCH*H*CH), 3.14 (s, 3H, OC*H*$_3$), 3.01 (dd, *J* = 5.0 Hz, *J* = 12.2 Hz, 1H, SeC*H*HCH), 1.15 (s, 9H, C(C*H*$_3$)$_3$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.6 (*C*), 142.4 (*C*), 139.4 (*C*H), 132.9 (*C*H), 130.5 (*C*H), 127.6 (*C*H), 127.2 (*C*H), 126.5 (*C*H), 125.6 (*C*H), 123.4 (*C*), 81.8 (*C*HOCH$_3$), 57.2 (*C*(CH$_3$)$_3$), 55.1 (O*C*H$_3$), 36.2 (Se*C*H$_2$CH), 22.3 (C(*C*H$_3$)$_3$) ppm.

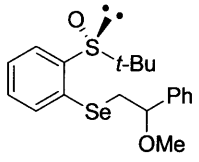
Minor isomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 1.4 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.43 (dd, *J* = 1.0 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.36 (dt, *J* = 1.3 Hz, *J* = 7.6 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.23–7.27 (m, 6H, Ar*H*), 4.24–4.28 (m, 1H, C*H*OCH$_3$), 3.22 (dd, *J* = 9.2 Hz, *J* = 12.1 Hz, 1H, SeC*H*HCH), 3.17 (s, 3H, OC*H*$_3$), 3.03–3.05 (m, 1H, SeCH*H*CH), 1.15 (s, 9H, C(C*H*$_3$)$_3$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.1 (*C*), 142.5 (*C*), 139.5 (*C*H), 132.9 (*C*H), 130.6 (*C*H), 127.6 (*C*H), 127.3 (*C*H), 126.6 (*C*H), 125.6 (*C*H), 123.4 (*C*), 81.8 (*C*HOCH$_3$), 57.3 (*C*(CH$_3$)$_3$), 55.1 (O*C*H$_3$), 36.2 (Se*C*H$_2$CH), 22.3 (C(*C*H$_3$)$_3$) ppm.

$C_{19}H_{24}SO_2Se$: 396 g/mol.

8.5.2.4 (*S*)-*t*-Butyl[2-{(2-methoxy-2-phenyl)ethyl]seleno}phenyl]sulfoxide (103a)



Synthesised according to GP 3 with 52 mg (0.1 mmol) (*S*)-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 34 µl styrene (0.30 mmol, 31 mg) in tetrahydrofuran with 100 µl dry methanol. After column chromatography (hexane/ethyl acetate, 5:1→1:1) the product was isolated as a mixture of diastereomers (*d.r.*: 5:1) in 50% yield (40 mg, 0.10 mmol) as pale yellow oil.

R_f (EA/Hex 1:3) = 0.20.

IR (film): $\tilde{\nu}$ = 3056, 2934, 1643, 1570, 1443, 1267, 1151, 1102, 1030, 958, 851, 738, 703, 640, 591 cm^{-1}.

MS (ES+) m/z (%): 815 (20), 793 ($[2M+NH_4]^+$, 25), 752 (3), 664 (5), 455 (13), 419 (19), 397 ($[M+NH_4]^+$, 100), 309 (14), 261 (10), 216 (18).

HRMS (ES+) $[M+NH_4]^+$: calculated for $C_{19}H_{25}O_2S^{74}Se$: 391.0795; found 391.0800.

$[\alpha]_{20}^{D}$ = –127.7° (c = 0.44, CH_2Cl_2).

Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 1.4 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.48 (dd, *J* = 1.0 Hz, *J* = 7.7 Hz, 1H, Ar*H*), 7.36 (ddd, *J* = 1.3 Hz, *J* = 7.6 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.24–7.27 (m, 6H, Ar*H*), 4.28 (dd, *J* = 5.0 Hz, *J* = 8.3 Hz, 1H, C*H*OCH$_3$), 3.29 (dd, *J* = 8.3 Hz, *J* = 12.1 Hz, 1H, SeC*H*HCH), 3.14 (s, 3H, OC*H*$_3$), 3.01 (dd, *J* = 12.2 Hz, *J* = 5.0 Hz, 1 H, SeCH*H*CH), 1.15 (s, 9H, C(C*H*$_3$)$_3$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.5 (*C*), 142.4 (*C*), 139.4 (*C*), 132.9 (*C*H), 130.5 (*C*H), 127.6 (*C*H), 127.2 (*C*H), 126.5 (*C*H), 125.6 (*C*H), 123.4 (*C*), 81.8 (*C*HOCH$_3$), 57.2 (*C*(CH$_3$)$_3$), 55.1 (O*C*H$_3$), 36.2 (Se*C*H$_2$CH), 22.3 (C(*C*H$_3$)$_3$] ppm.

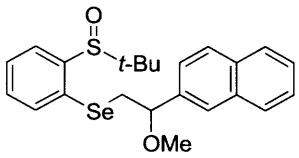
Minor isomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 1.4 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.43 (dd, *J* = 1.0 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.36 (ddd, *J* = 1.3 Hz, *J* = 7.8 Hz, *J* = 7.6 Hz, 1H, Ar*H*), 7.24–7.28 (m, 6H, Ar*H*), 4.25–4.27 (m, 1H, C*H*OCH$_3$), 3.22 (dd, *J* = 9.2 Hz, *J* = 12.1 Hz, 1H, SeC*H*HCH), 3.17 (s, 3H, OC*H*$_3$), 3.04 (m, 1H, SeCH*H*CH), 1.15 (s, 9H, C(C*H*$_3$)$_3$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.0 (*C*), 142.5 (*C*), 139.5 (*C*H), 132.9 (*C*H), 130.6 (*C*H), 127.6 (*C*H), 127.3 (*C*H), 126.6 (*C*H), 125.6 (*C*H), 123.4 (*C*), 81.8 (*C*HOCH$_3$), 57.3 (*C*(CH$_3$)$_3$), 55.1 (O*C*H$_3$), 36.2 (Se*C*H$_2$CH), 22.3 (C(*C*H$_3$)$_3$) ppm.

$C_{19}H_{24}SO_2Se$: 396 g/mol.

8.5.2.5 *rac-t*-Butyl[2-{(2-methoxy-2-naphthyl)ethyl]seleno}phenyl]sulfoxide (104)



Synthesised according to GP 3 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 34 mg 2-vinylnaphthalene (0.22 mmol) in tetrahydrofuran with 100 µl dry methanol. After column chromatography (hexane/ethyl acetate, 5:1→1:1) the product was isolated as a mixture of diastereomers (*d.r.*: 5:1) in 32% yield (29 mg, 0.064 mmol) as colourless oil.

R_f (EA/Hex 1:1) = 0.20.

IR (film): $\tilde{\nu}$ = 2928, 1711, 1598, 1445, 1366, 1262, 1153, 1095, 1045, 753 cm^{-1}.

MS (ES+): m/z (%): 893 ($[2M+H]^+$, 34), 796 (4), 469 (5), 447 ($[M+H]^+$, 100), 359 (12), 260 (7).

HRMS (ES+): $[M+H]^+$ calculated for $C_{23}H_{27}O_2S^{80}Se$: 447.0891; found 447.0886.

Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88–7.69 (m, 5H, Ar*H*), 7.57 (dd, *J* = 1.1 Hz, *J* = 7.7 Hz, 1H, Ar*H*), 7.53–7.46 (m, 2H, Ar*H*), 7.46–7.37 (m, 2H, Ar*H*), 7.37–7.27 (m, 1H, Ar*H*), 4.50 (dd, *J* = 5.5 Hz, *J* = 7.9 Hz, 1H, C*H*OCH_3), 3.45 (dd, *J* = 8.0 Hz, *J* = 12.2 Hz, 1H, SeC*H*HCH), 3.25 (s, 3H, OCH_3), 3.15 (dd, *J* = 5.5 Hz, *J* = 12.2 Hz, 1H, SeCH*H*CH), 1.21 (s, 9H, C(CH_3)$_3$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 151.5 (*C*), 143.6 (*C*), 137.8 (*C*H), 133.9 (*C*H), 133.3 (*C*), 133.1 (*C*H), 131.6 (*C*H), 131.4 (*C*H), 128.6 (*C*H), 127.9 (*C*H), 127.7 (*C*), 127.5 (*C*H), 127.5 (*C*H), 126.3 (*C*H), 126.1 (*C*), 123.9 (*C*H), 83.1 (*C*HOCH_3), 58.2 (*C*$(CH_3)_3$), 57.2 (O*C*H_3), 36.8 (Se*C*H_2CH), 23.3 (C(*C*H_3)$_3$) ppm.

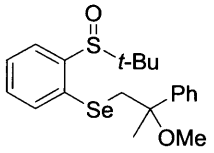
Minor isomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88–7.69 (m, 5H, ArH), 7.57 (dd, *J* = 1.1 Hz, *J* = 7.7 Hz, 1H, ArH), 7.53–7.46 (m, 2H, ArH), 7.46–7.37 (m, 2H, ArH), 7.37–7.27 (m, 1H, ArH), 4.50 (m, 1H, C*H*OCH_3), 3.39 (dd, *J* = 9.2 Hz, *J* = 12.1 Hz, 1H, SeCH*H*CH), 3.29 (s, 3H, OCH_3), 3.18 (m, 1H, SeC*H*HCH), 1.23 (s, 9H, C(CH_3)$_3$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 151.3 (*C*), 143.4 (*C*), 137.9 (*C*H), 133.9 (*C*H), 133.5 (*C*), 133.2 (*C*H), 132.1 (*C*H), 131.3 (*C*H), 128.5 (*C*H), 127.9 (*C*H), 127.7 (*C*), 127.4 (*C*H), 127.2 (*C*H), 126.3 (*C*H), 125.9 (*C*), 123.9 (*C*H), 83.0 (*C*HOCH_3), 58.2 (*C*$(CH_3)_3$), 57.0 (O*C*H_3), 37.3 (Se*C*H_2CH), 23.3 (C(*C*H_3)$_3$) ppm.

$C_{23}H_{26}SO_2Se$: 446 g/mol.

8.5.2.6 *rac*-*t*-Butyl[2-{(2-methoxy-2-methyl-2-phenyl)ethyl]seleno}phenyl]sulfoxide (105)



Synthesised according to GP 3 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 39 µl α-methylstyrene (0.30 mmol, 35 mg) in dichloromethane with 100 µl dry methanol. After column chromatography (hexane/ethyl acetate, 5:1→1:1) the product was isolated as a mixture of diastereomers (*d.r.*: 4:1) in 38% yield (31 mg, 0.076 mmol) as colourless oil.

R_f (EA/Hex 1:3) = 0.18.

MS (ES+): m/z (%): 821 ($[2M+H]^+$, 50), 433 (6), 411 ($[M+H]^+$, 100), 379 (22), 323 (12), 260 (29), 204 (6).

HRMS (ES+): $[M+H]^+$ calculated for $C_{23}H_{27}O_2S^{80}Se$: 411.0891; found 411.0889.

IR (film): $\tilde{\nu}$ = 3054, 2976, 2824, 1571, 1492, 1445, 1422, 1362, 166, 1073, 1046, 1022, 868, 763, 701 cm^{-1}.

Major isomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 1.0 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.44 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.20–7.40 (m, 7H, Ar*H*), 3.43 (d, *J* = 11.6 Hz, 1H, $SeCH_2CH$), 3.17 (d, *J* = 11.6 Hz, 2H, $SeCH_2CH$), 3.07 (s, 3H, OCH_3), 1.68 (s, 3H, CH_3), 1.16 (s, 9H, $C(CH_3)_3$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.3 (*C*), 143.3 (*C*), 134.2 (*C*H), 132.3 (*C*), 131.4 (*C*H), 128.4 (*C*H), 127.4 (*C*H), 127.2 (*C*H), 126.2 (2*C*H), 121.3 (*C*H), 78.9 ($COCH_3$), 58.2 ($C(CH_3)_3$), 51.1 (OCH_3), 44.2 ($SeCH_2CH$), 24.2 (CCH_3), 23.4 ($C(CH_3)_3$) ppm.

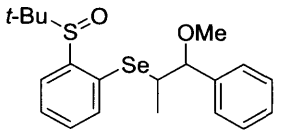
Minor Isomer:

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 1.0 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.20–7.40 (m, 8H, Ar*H*), 3.37 (d, *J* = 11.61 Hz, 2H, $SeCH_2CH$), 3.19 (d, *J* = 11.63 Hz, 1H, $SeCH_2CH$), 3.09 (s, 3H, OCH_3), 1.68 (s, 3H, CH_3), 1.17 (s, 9H, $C(CH_3)_3$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.3 (*C*), 143.7 (*C*), 134.0 (*C*H), 132.6 (*C*), 131.3 (*C*H), 128.4 (*C*H), 127.5 (*C*H), 127.2 (*C*H), 126.1 (2*C*H), 121.3 (*C*H), 78.9 ($COCH_3$), 58.1 ($C(CH_3)_3$), 51.1 (OCH_3), 44.2 ($SeCH_2CH$), 24.2 (CCH_3), 23.5 ($C(CH_3)_3$) ppm.

$C_{20}H_{26}SO_2Se$: 409 g/mol.

8.5.2.7 *rac-t*-Butyl[2-{(2-Methoxy-1-methyl-2-phenyl)ethyl]seleno}phenyl]sulfoxide (106)



Synthesised according to GP 3 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 26 mg *β*-methylstyrene (0.22 mmol) in dichloromethane with 100 µl dry methanol. After column chromatography (hexane/ethyl acetate, 5:1→1:1) the product was isolated as a mixture of diastereomers (*d.r.*: 11:1) in 30% yield (25 mg, 0.06 mmol) as colourless oil.

R_f (EA/Hex 1:3) = 0.14.

MS (ES+) m/z (%): 821 ($[2M+H]^+$, 2), 411 ($[M+H]^+$, 100), 323 (25), 204 (16).

HRMS (ES+): $[M+H]^+$ calculated for $C_{20}H_{27}O_2S^{74}Se$: 405.0951; found 405.0960.

IR (film): $\tilde{\nu}$ = 2975, 2927, 1445, 1125, 1080, 1045, 1022, 755, 702 cm^{-1}.

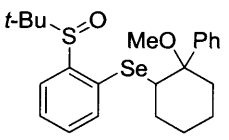
Minor isomer is indicated by: *

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 1.4 Hz, *J* = 7.9 Hz, 1H, Ar*H*), 7.81 (dd, *J* = 1.4 Hz, *J* = 7.9 Hz, 1H, Ar*H*)*, 7.60–7.62 (m, 1H, Ar*H*)*, 7.59 (dd, *J* = 1.1 Hz, *J* = 7.7 Hz, 1H, Ar*H*), 7.47 (dt, *J* = 1.3 Hz, *J* = 7.6 Hz, 1H, Ar*H*), 7.34–7.39 (m, 3H, Ar*H*), 7.26–7.32 (m, 3H, Ar*H*), 4.41 (d, *J* = 4.7 Hz, 1H, SeC*H*CH), 4.32 (d, *J* = 4.3 Hz, 1H, SeC*H*CH)*, 3.52 (dq, *J* = 4.7 Hz, *J* = 7.0 Hz, 1H, SeCHC*H*), 3.29 (s, 3H, OCH_3)*, 3.28 (s, 3H, OCH_3), 1.31 (d, *J* = 7.0 Hz, 3H, CH_3), 1.21 (s, 9H, C(CH_3)$_3$)*, 1.21 (s, 9H, C(CH_3)$_3$) ppm.

^{13}C NMR (500 MHz, $CDCl_3$): δ = 156.3* (*C*), 153.8 (*C*), 144.8 (*C*), 139.1 (*C*H), 135.5 (*C*H), 135.5* (*C*H), 131.2 (*C*), 131.0* (*C*), 128.3 (*C*H), 128.2* (*C*H), 127.9 (*C*H), 127.8 (*C*H), 127.6 (*C*H), 127.0 (*C*H), 126.9* (*C*H), 86.2 (*C*OCH$_3$), 58.3 (*C*(CH$_3$)$_3$), 57.4 (OCH$_3$), 48.6 (Se*C*HCH) 23.4 (C(*C*H$_3$)$_3$), 16.6 (SeCH*C*H$_3$) ppm.

$C_{20}H_{26}SO_2Se$: 409 g/mol.

8.5.2.8 *rac-t*-Butyl[2-{(2-methoxy-2-phenyl)cyclohexyl]seleno}phenyl]sulfoxide (107)



Synthesised according to GP 3 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 48 µl 1-phenyl-1-cyclohexene (0.30 mmol, 48 mg) in dichloromethane with 100 µl dry methanol. After

column chromatography (hexane/ethyl acetate, 5:1→1:1) the product was isolated as a mixture of diastereomers (*d.r.*: 9:1) in 30% yield (27 mg, 0.06 mmol) as colourless oil.

R_f (EA/Hex 1:3) = 0.11.

MS (ES+) m/z (%): 901 ($[2M+H]^+$, 50), 580 (16), 451 ($[M+H]^+$, 100), 419 (66), 363 (14), 260 (7).

HRMS (ES+): $[M+H]^+$ calculated for $C_{20}H_{27}O_2S^{80}Se$: 451.1204; found 451.1197.

IR (film): $\tilde{\nu}$ = 2935, 2857, 1445, 1361, 1209, 1151, 1065, 1047, 1020, 880, 758, 699 cm^{-1}.

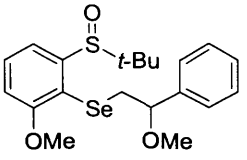
Minor isomer is indicated by: *

^1H NMR (500 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 1.4 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.33 (m, 6H, Ar*H*), 7.40–7.29 (m, 6H, Ar*H*)*, 7.12 (dt, *J* = 1.5, *J* = 7.5 Hz, 1H, Ar*H*), 6.85 (dd, *J* = 1.0 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 3.66 (s, 1H, ArSeC*H*), 3.60 (s, 1H, ArSeC*H*)*, 2.88 (s, 3H, OCH_3), 2.86 (s, 3H, OCH_3)*, 2.16 (dd, *J* = 3.4 Hz, *J* = 9.6 Hz, 2H), 1.73–1.66 (m, 3H)*, 1.69 (m, 3H), 1.60 (m, 3H), 1.12 (s, 9H, C(CH_3)$_3$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.0* (*C*), 154.2 (*C*), 144.7 (*C*), 143.7 (*C*), 135.8 (*C*H), 131.0 (*C*H), 130.9 (*C*H), 128.1 (*C*H), 127.6 (*C*H), 127.5* (*C*H), 127.2 (*C*H), 126.8 (*C*H), 79.1 (*C*OCH$_3$), 58.5 (*C*(CH$_3$)$_3$), 58.3 (OCH$_3$), 50.1 (ArSe*C*H), 27.9 (*C*H$_2$), 26.0 (*C*H$_2$), 23.5 (C(*C*H$_3$)$_3$), 21.3 (*C*H$_2$), 20.7 (*C*H$_2$) ppm.

$C_{23}H_{30}SO_2Se$: 450 g/mol.

8.5.2.9 *rac*-2-(*t*-Butylsulfinyl)-6-methoxyphenyl 2-methoxy-2-phenylethyl selenide (108)



Synthesised according to GP 3 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)-6-methoxyphenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 38 µl styrene (0.30 mmol, 42 mg) in chloroform at –50 °C with 100 µl dry methanol. After column chromatography (hexane/ethyl acetate, 5:1→1:1) the product was isolated as a mixture of diastereomers (*d.r.*: 2:1) in 24% yield (20 mg, 0.048 mmol) as colourless oil.

R_f (E) = 0.26.

MS (ES+) m/z (%): 490 ($[M+Na+acetonitrile]^+$, 100), 449 ($[M+Na]^+$, 80), 427 ($[M+H]^+$,75), 425 (40), 380 (15), 339 (30), 276 (35), 130 (25), 85 (38).

HRMS (ES+): $[M+H]^+$ calculated for $C_{20}H_{27}O_3S^{80}Se$ 427.0846; found 427.0865.

IR (film): $\tilde{\nu}$ = 2936, 1568, 1492, 1455, 1429, 1360, 1286, 1260, 1169, 1149, 1104, 1040, 1026, 957, 833, 786, 768, 702 cm^{-1}.

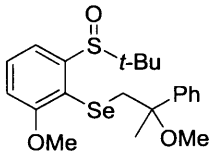
Isomer is indicated by: *.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (m, 2H, Ar*H*), 7.35 (m, 1H, Ar*H*), 7.28 (m, 3H, Ar*H*), 7.22 (m, 1H, Ar*H*), 6.97 (dd, *J* = 2.6 Hz, *J* = 6.7 Hz, 1H, Ar*H*), 6.94 (dd, *J* = 3.0 Hz, *J* = 6.2 Hz, 1H, Ar*H*)*, 4.39 (dd, *J* = 5.3 Hz, *J* = 8.3 Hz, 1H, C*H*OCH_3), 4.18 (dd, *J* = 4.2 Hz, *J* = 9.4 Hz, 1H, C*H*OCH_3)*, 3.95 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3)*, 3.32 (dd, *J* = 8.4 Hz, *J* = 12.0 Hz, 1H, SeC*H*HCH), 3.22 (s, 3H, OCH_3)*, 3.19 (s, 3H, OCH_3), 3.13 (dd, *J* = 4.6 Hz, *J* = 7.6 Hz, 1H, SeC*H*HCH)*, 3.04 (dd, *J* = 4.2 Hz, *J* = 12.2 Hz, 1H, SeCH*H*CH)*, 2.89 (dd, *J* = 5.3 Hz, *J* = 12.0 Hz, 1H, SeCH*H*CH), 1.22 (s, 9H, $C(CH_3)_3$)*, 1.20 (s, 9H, $C(CH_3)_3$) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.1 (*C*), 140.8 (*C*), 129.4 (2*C*H), 128.5 (*C*H), 128.1 (*C*H), 127.9* (*C*H), 126.6 (*C*H), 126.4 (*C*H), 119.6 (*C*), 112.6 (*C*H), 112.5* (*C*H), 83.8 (*C*HOCH_3), 58.2 (*C*$(CH_3)_3$), 57.1* (OCH_3), 56.9 (OCH_3), 56.2 (OCH_3), 56.2* (OCH_3), 36.0 (Se*C*H_2CH), 23.5 ($C(CH_3)_3$) ppm.

$C_{20}H_{26}SO_3Se$: 425 g/mol.

8.5.2.10 *rac*-2-(*t*-Butylsulfinyl)-6-methoxyphenyl 2-methoxy-2-phenylpropyl selenide (109)



Synthesised according to GP 3 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)-6-methoxyphenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 39 µl α-methylstyrene (0.30 mmol, 35 mg) in chloroform at –50 °C with 100 µl dry methanol. After column chromatography (hexane/ethyl acetate, 5:1→1:1) the product was isolated as a mixture of diastereomers (*d.r.*: 1:1) in 22% yield (19 mg, 0.044 mmol) as colourless oil.

R_f (E) = 0.19.

MS (ES+) m/z (%): 504 (12), 463 ($[M+Na]^+$, 100), 449 ($[M+H]^+$, 5), 415 (10).

HRMS (ES+): $[M+Na]^+$ calculated $C_{21}H_{28}O_3SNa^{80}Se$ 463.0822; found 463.0831.

IR (film): $\tilde{\nu}$ = 3059, 1568, 1493, 1455, 1429, 1362, 1286, 1261, 1167, 1149, 1092, 1072, 1040, 1026, 911, 834, 786, 766, 701 cm^{-1}.

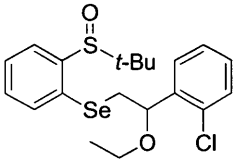
Isomer is indicated by: *.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20–7.50 (m, 7H, Ar*H*), 6.94 (dd, *J* = 2.6 Hz, *J* = 6.8 Hz, 1H, Ar*H*), 6.87 (dd, *J* = 2.7 Hz, *J* = 6.7 Hz, 1H, Ar*H*)*, 3.91 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3)*, 3.45 (d, *J* = 11.0 Hz, 1H, SeCH*H*)*, 3.32 (d, *J* = 11.5 Hz, 1H, SeCH*H*), 3.20 (d, *J* = 11.5 Hz, 1H, SeC*H*H), 3.12–3.14 (m, 1H, SeC*H*H)*, 3.11 (s, 3H, OCH_3)*, 3.07 (s, 3H, OCH_3), 1.72 (s, 3H, CH_3), 1.72 (s, 3H, CH_3)*, 1.19 (s, 9H, $C(CH_3)_3$)*, 1.18 (s, 9H, $C(CH_3)_3$) ppm.

^{13}C NMR (63 MHz, $CDCl_3$): δ = 159.1 (Ar*C*-OCH_3), 143.5 (Ar*C*), 143.5* (Ar*C*), 129.4, 129.2, 128.2, 128.2*, 127.3, 127.3*, 126.1, 126.0*, 119.6, 119.6, 119.5*, 112.5, 112.4*, 79.0, 79.0*, 58.2, 56.2, 56.1*, 50.9, 42.5, 42.0*, 30.3, 23.5 ($C(CH_3)_3$), 23.4* ($C(CH_3)_3$) ppm.

$C_{21}H_{28}SO_3Se$: 439 g/mol.

8.5.2.11 *rac-t*-Butyl[2-{(2-ethoxy-2-(2-chloro)phenyl)ethyl]seleno}phenyl]sulfoxide (110)



Synthesised according to GP 3 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 38 µl 2-chlorostyrene (0.30 mmol, 42 mg) in dichloromethane with 100 µl dry ethanol. After column chromatography (hexane/ethyl acetate, 5:1→1:1) the product was isolated as a mixture of diastereomers (*d.r.*: 8:1) in 47% yield (42 mg, 0.094 mmol) as colourless oil.

MS (ES+) m/z (%): 445 ($[M+H]^+$, 100), 391 (28), 343 (25), 261 (8), 204 (16).

HRMS (ES+): $[M+H]^+$ calculated for $C_{20}H_{26}O_2{}^{35}ClS^{74}Se$ 439.0561; found 439.0569.

IR (film): $\tilde{\nu}$ = 2973, 2926, 1572, 1471, 1442, 1362, 1168, 1119, 1096, 1048, 1023, 908, 756, 733, 591 cm^{-1}.

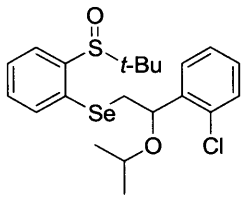
Minor isomer is indicated by: *.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (dd, *J* = 1.4 Hz, *J* = 7.9 Hz, 1H, Ar*H*)*, 7.77 (dd, *J* = 1.5 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.62 (dd, *J* = 1.2 Hz, *J* = 7.7 Hz, 1H, Ar*H*), 7.58 (dd, *J* = 1.1 Hz, *J* = 7.8 Hz, 1H, Ar*H*)*, 7.51 (m, 1H, Ar*H*)*, 7.49 (dd, *J* = 1.6 Hz, *J* = 8.0 Hz, 1H, Ar*H*), 7.41 (dt, *J* = 1.3 Hz, *J* = 7.6 Hz, 1H, Ar*H*), 7.34 (dt, *J* = 1.5 Hz, *J* = 7.5 Hz, 1H, Ar*H*), 7.26–7.29 (m, 2H, Ar*H*), 7.19 (m, 1H, Ar*H*), 4.97 (dd, *J* = 3.6 Hz, *J* = 8.7 Hz, 1H, C*H*OCH_2CH_3), 4.84 (dd, *J* = 3.3 Hz, *J* = 9.3 Hz, 1H, C*H*O CH_2CH_3)*, 3.41 (m, 2H, CH_2CH_3), 3.23 (m, 1H, SeC*H*HCH), 3.15 (dd, *J* = 3.7 Hz, *J* = 12.5 Hz, 1H, SeC*H*HCH), 3.08 (dd, *J* = 9.3 Hz, *J* = 12.4 Hz, 1H, SeCH*H*CH)*, 1.23 (s, 9H, $C(CH_3)_3$), 1.18 (t, *J* = 7.0 Hz, 3H, CH_2CH_3) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.2 (*C*), 138.6 (*C*), 134.0 (*C*H), 132.6 (*C*), 131.9 (*C*), 131.9* (*C*), 131.2 (*C*H), 129.5* (*C*H), 129.4 (*C*H), 129.0* (*C*H), 128.9 (*C*H), 127.4 (*C*H), 127.3 (*C*H), 127.3* (*C*H), 127.2 (*C*H), 127.2 (*C*H), 77.5 ($SeCH_2CH$), 65.3* (OCH_2CH_3), 65.1 (OCH_2CH_3), 58.2 ($C(CH_3)_3$), 35.9* (ArSe*C*H), 35.7 (ArSe*C*H), 23.3 ($C(CH_3)_3$), 23.2* ($C(CH_3)_3$), 15.2* (OCH_2CH_3), 15.1 (OCH_2CH_3) ppm.

$C_{20}H_{25}ClSO_2Se$: 444 g/mol.

8.5.2.12 *rac-t*-Butyl[2-{(2-*i*-propyloxy-2-(2-chloro)phenyl)ethyl]seleno}phenyl]sulfoxide (111)



Synthesised according to GP 3 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 38 µl 2-chlorostyrene (0.30 mmol, 42 mg) in dichloromethane with 100 µl dry *i*-propanol. After column chromatography (hexane/ethyl acetate, 5:1→1:1), the product was isolated as a mixture of diastereomers (*d.r.*: 8:1) in 47% yield (43 mg, 0.094 mmol) as colourless oil.

MS (ES+) m/z (%): 481 (7), 459 ([M+H$^+$, 100), 391 (28), 343 (13), 199 (14).

HRMS (ES+): $[M+H]^+$ calculated for $C_{21}H_{28}O_2{}^{35}ClS^{74}Se$ 453.0718; found 453.0722.

IR (film): $\tilde{\nu}$ = 2971, 2928, 1572, 1470, 1443, 1378, 1363, 1329, 1166, 1120, 1087, 1048, 1023, 941, 756, 705 cm^{-1}.

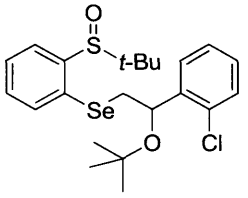
Minor isomer is indicated by: *.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (dd, *J* = 1.5 Hz, *J* = 7.9 Hz, 1H, Ar*H*)*, 7.77 (dd, *J* = 1.5 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.62 (dd, *J* = 1.2 Hz, *J* =7.7 Hz, 1H, Ar*H*), 7.58 (dd, *J* = 1.2 Hz, *J* = 7.8 Hz, 1H, Ar*H*)*, 7.54 (dd, *J* = 1.6 Hz, *J* = 8.1 Hz, 1H, Ar*H*), 7.40 (dt, *J* = 1.3 Hz, *J* = 7.6 Hz, 1H, Ar*H*), 7.33 (dt, *J* = 1.5 Hz, *J* = 7.5 Hz, 1H, Ar*H*), 7.26–7.30 (m, 2H, Ar*H*), 7.18–7.21 (m, 1H, Ar*H*), 5.11 (dd, *J* = 3.4 Hz, *J* = 9.0 Hz, 1H, $SeCH_2CH$), 4.99–5.01 (m, 1H, $SeCH_2CH$)*, 3.51 (sept, *J* = 6.1 Hz, 1H, $CHOCH(CH_3)_2$), 3.24 (dd, *J* = 9.1 Hz, *J* = 12.4 Hz, 1H, SeC*H*HCH), 3.24 (dd, *J* = 9.1 Hz, *J* = 12.4 Hz, 1H, SeC*H*HCH)*, 3.10 (dd, *J* = 3.5 Hz, *J* = 12.3 Hz, 1H, SeCH*H*CH), 1.23 (s, 9H, $C(CH_3)_3$), 1.23 (s, 9H, $C(CH_3)_3$)*, 1.08 (d, *J* = 6.4 Hz, 6H, $CHOCH(CH_3)_2$)*, 1.07 (d, *J* = 6.2 Hz, 6H, $CHOCH(CH_3)_2$) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.4 (*C*), 140.0 (*C*), 134.2 (*C*H), 134.0* (*C*H), 132.8 (*C*), 132.8 (*C*), 131.7 (*C*H), 129.8 (*C*H), 129.3 (*C*H), 128.0 (*C*H), 127.8 (*C*H), 127.7 (*C*H), 127.6 (*C*H), 127.6* (*C*H), 75.4 ($SeCH_2CH$), 71.2* ($OCH(CH_3)_2$), 70.9 ($OCH(CH_3)_2$), 58.7 ($C(CH_3)_3$), 36.6 ($ArSeCH_2$), 23.8 ($C(CH_3)_3$), 23.6* ($C(CH_3)_3$), 22.0* ($OCH(CH_3)_2$), 21.9 ($OCH(CH_3)_2$) ppm.

$C_{21}H_{27}ClSO_2Se$: 458 g/mol.

8.5.2.13 *rac-t*-Butyl[2-{(2-*t*-butyloxy-2-(2-chloro)phenyl)ethyl]seleno}phenyl]sulfoxide (112)



Synthesised according to GP 3 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 38 µl 2-chlorostyrene (0.30 mmol, 42 mg) in dichloromethane with 100 µl dry *t*-butanol. After column chromatography (hexane/ethyl acetate, 5:1→1:1) the product was isolated as a mixture of diastereomers (*d.r.*: 6:1) in 30% yield (28 mg, 0.060 mmol) as colourless oil.

MS (ES+) m/z (%): 945 (38), 495 (7), 473 ($[M+H]^+$, 100), 417 (44), 343 (21), 260 (16), 205 (12).

HRMS (ES+): $[M+H]^+$ calculated for $C_{22}H_{30}O_2{}^{35}ClS^{74}Se$ 467.0874; found 467.0877.

IR (film): $\tilde{\nu}$ = 2972, 1470, 1443, 1365, 1187, 1082, 1047, 1022, 755 cm^{-1}.

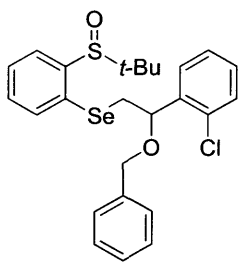
Minor isomer is indicated by: *.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (dd, *J* = 1.5 Hz, *J* = 7.9 Hz, 1H, Ar*H*)*, 7.75–7.78 (m, 1H, Ar*H*), 7.61–7.67 (m, 2H, Ar*H*), 7.58 (dd, *J* = 1.2 Hz, *J* = 7.7 Hz, 1H, Ar*H*)*, 7.38–7.42 (m, 1H, ArH), 7.31–7.36 (m, 1H, Ar*H*), 7.23–7.29 (m, 2H, Ar*H*), 7.13–7.18 (m, 1H, Ar*H*), 5.21 (dd, *J* = 3.5 Hz, *J* = 8.9 Hz, 1H, C*H*OC$(CH_3)_3$), 5.14 (dd, *J* = 3.3 Hz, *J* = 9.1 Hz, 1H, C*H*OC$(CH_3)_3$)*, 3.24 (dd, *J* = 8.9 Hz, *J* = 12.3 Hz, 1H, SeC*H*HCH), 3.19 (m, 1H, SeC*H*HCH)*, 3.03 (dd, *J* = 3.6 Hz, *J* = 12.3 Hz, 1H, SeCH*H*CH), 1.23 (s, 9H, C(C*H*$_3)_3$), 1.12 (s, 9H, C(C*H*$_3)_3$) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.5 (*C*), 133.7 (*C*H), 133.4 (*C*), 133.3 (*C*), 131.7 (*C*H), 131.5 (*C*), 129.6 (*C*H), 129.0 (*C*H), 128.7 (*C*H), 127.8 (*C*H), 127.5 (*C*H), 127.4 (*C*H), 75.6 (O*C*$(CH_3)_3$), 70.6 (SeCH$_2$*C*H), 58.7 (*C*$(CH_3)_3$), 37.6 (ArSe*C*H$_2$), 29.0 (OC(*C*H$_3)_3$), 23.8 (C(*C*H$_3)_3$) ppm.

$C_{22}H_{29}ClSO_2Se$: 472 g/mol.

8.5.2.14 *rac-t*-Butyl[2-{(2-benzyloxy-2-(2-chloro)phenyl)ethyl]seleno}phenyl]sulfoxide (113)



Synthesised according to GP 3 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 38 µl

2-chlorostyrene (0.30 mmol, 42 mg) in dichloromethane with 100 µl dry benzyl alcohol. After column chromatography (hexane/ethyl acetate, 5:1→1:1) the product was isolated as a mixture of diastereomers (*d.r.*: 3.5:1) in 30% yield (30 mg, 0.060 mmol) as colourless oil.

MS (ES+) m/z (%): 1013 ($[2M+H]^+$, 15), 507 ($[M+H]^+$, 100), 391 (12), 342 (22), 204 (13).

HRMS (ES+): $[M+H]^+$ calculated for $C_{25}H_{28}O_2{}^{35}ClS^{74}Se$ 501.0717; found 501.0718.

IR (film): $\tilde{\nu}$ = 3060, 3029, 2973, 2925, 2864, 1570, 1471, 1441, 1361, 1167, 1089, 1047, 1024, 755 cm^{-1}.

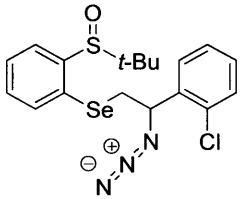
Minor isomer is indicated by: *.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 1.3 Hz, *J* = 7.9 Hz, 1H, Ar*H*)*, 7.67 (dd, *J* = 1.4 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.49–7.51 (m, 1H, Ar*H*), 7.46 (dd, *J* = 1.1 Hz, *J* = 7.8 Hz, 1H, Ar*H*)*, 7.42 (dd, *J* = 1.1 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.35–7.37 (m, 1H, Ar*H*)*, 7.30–7.32 (m, 1H, Ar*H*), 7.18–7.29 (m, 9H, Ar*H*), 5.00 (dd, *J* = 3.5 Hz, *J* = 8.7 Hz, 1H, C*H*OCH$_2$Ar), 4.95–4.97 (m, 1H, C*H*OCH$_2$Ar)*, 4.33–4.35 (m, 2H CHOC*H*$_2$Ar), 3.22 (dd, *J* = 8.7 Hz, *J* = 12.6 Hz, 1H, SeC*H*HCH), 3.08 (dd, *J* = 3.6 Hz, *J* = 12.6 Hz, 1H, SeCH*H*CH), 1.14 (s, 9H, (C(C*H*$_3$)$_3$)) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.2 (C), 138.0, 137.5, 134.0, 132.8, 131.7, 131.3*, 131.2, 129.6*, 129.6, 129.1, 128.3, 128.0, 127.9, 127.9*, 127.8, 127.7*, 127.4, 127.4, 127.3, 127.3*, 127.3*, 71.6, 71.3, 58.2 (*C*(CH$_3$)$_3$), 35.9*, 35.5, 23.3 (C(*C*H$_3$)$_3$) ppm.

$C_{25}H_{27}ClSO_2Se$: 505 g/mol.

8.5.2.15 *rac*-2-Azido-2-(2-chlorophenyl)ethyl-2-(*t*-butylsulfinyl)phenyl selenide (114)



Synthesised according to GP 3 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 38 µl 2-chlorostyrene (0.30 mmol, 42 mg) in dichloromethane with 20 µl (0.20 mmol, 23 mg) dry trimethylsilyl azide. After column chromatography (hexane/ethyl acetate, 5:1→1:1) the product was isolated as a mixture of diastereomers (*d.r.*: 6:1) in 35% yield (31 mg, 0.070 mmol) as colourless oil.

R_f (EA/Hex 1:3) = 0.37.

MS (ES+): m/z (%): 442 ($[M+H]^+$, 100), 368 (20), 343 (40), 261 (2), 205 (21).

HRMS (ES+) $[M+H]^+$ calculated for $C_{18}H_{21}{}^{35}ClN_3OS^{76}Se$ 438.0281; found 438.0281.

IR (film): $\tilde{\nu}$ = 2963, 2925, 2107, 1472, 1443, 1249, 1046, 1021, 756 cm^{-1}.

Minor isomer is indicated by: *.

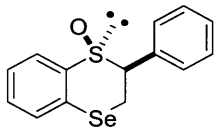
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (dd, *J* = 1.4 Hz, *J* = 7.9 Hz, 1H, Ar*H*)*, 7.79 (dd, *J* = 1.4 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.61 (dd, *J* = 1.1 Hz, *J* = 7.7 Hz, 1H, Ar*H*), 7.57 (dd, *J* = 1.1 Hz, *J* = 7.7 Hz, 1H, Ar*H*)*, 7.46 (tt, *J* = 1.9 Hz, *J* = 3.4 Hz, 2H, Ar*H*), 7.38 (dd, *J* = 1.4 Hz, *J* = 7.5 Hz, 1H, Ar*H*), 7.28–7.30 (m, 2H, Ar*H*), 7.23 (dd, *J* = 1.7 Hz, *J* = 7.6 Hz, 1H, Ar*H*), 7.20–7.22 (m, 1H, Ar*H*)*, 5.22 (dd, *J* = 4.6 Hz, *J* = 8.5 Hz, 1H, C*H*N_3), 3.31 (dd, *J* = 4.6 Hz, *J* = 12.6 Hz, 1H, SeC*H*HCH)*, 3.25 (dd, *J* = 4.6 Hz, *J* = 12.8 Hz, 1H, SeC*H*HCH), 3.18 (dd, *J* = 8.5 Hz, *J* = 12.8 Hz, 1H, SeCH*H*CH), 3.09 (dd, *J* = 9.1 Hz, *J* = 12.6 Hz, 1H, SeCH*H*CH)*, 1.22 (s, 9H, C(C*H*$_3$)$_3$) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.1 (*C*), 134.6(*C*), 134.3 (*C*), 132.5 (*C*H), 131.5 (*C*H), 130.1 (*C*), 129.9 (*C*H), 129.7 (*C*H), 128.1 (*C*H), 127.8 (*C*H), 127.6 (*C*H), 127.5 (*C*H), 62.1 (SeCH_2*C*HN_3), 58.4 (*C*$(CH_3)_3$), 34.3 (ArSe*C*H_2), 23.3 (C(*C*H_3)$_3$) ppm.

$C_{18}H_{20}ClN_3SOSe$: 441 g/mol.

8.5.3 Cyclisation Reaction

8.5.3.1 (*S**,*S**)-2-Phenyl-2,3-dihydro-1,4-benzoselenathiine-1-oxide (115)



Synthesised according to GP 4 with 52 mg (0.1 mmol) (*S*)-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 34 µl styrene (0.30 mmol, 31 mg) in tetrahydrofuran. After column chromatography (hexane/ethyl acetate, 4:1→1:1), the product was isolated in 10% yield (6 mg, 0.020 mmol) as colourless oil.

R_f (EA/Hex 1:3) = 0.25.

MS (ES+) m/z (%): 617 ($[2M+H]^+$: 10), 421 (10), 331 (15), 309 ($[M+H]^+$, 100), 205 (6).

HRMS (ES+): $[M+H]^+$: calculated for $C_{14}H_{13}OS^{76}Se$ 304.9874, found 304.9880.

IR (film): $\tilde{\nu}$ = 3057, 2928, 1575, 1494, 1452, 1425, 1251, 1093, 1063, 1049, 1030, 754, 728, 698 cm^{-1}.

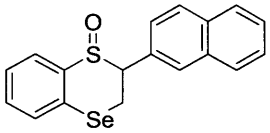
[α] $^{20}_{D}$ = +48.0° (c = 0.1, CH_2Cl_2).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.57 (dd, *J* = 0.9 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.47 (dd, *J* = 1.4 Hz, *J* = 7.7 Hz, 1H, Ar*H*), 7.37 (ddd, *J* = 1.5 Hz, *J* = 7.6 Hz, *J* = 7.7 Hz, 1H, Ar*H*), 7.29–7.23 (m, 4H, Ar*H*), 7.09 (dd, *J* = 1.8 Hz, *J* = 7.6 Hz, 2H, Ar*H*), 4.51 (dd, *J* = 6.2 Hz, *J* = 8.1 Hz, 1H, SeCH_2C*H*S), 3.88 (dd, *J* = 8.2 Hz, *J* = 11.7 Hz, 1H, SeC*H*HCHS), 3.33 (dd, *J* = 11.7 Hz, *J* = 6.1 Hz, 1 H, SeCH*H*CHS) ppm.

^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.5 (*C*), 134.7 (*C*H), 131.6 (*C*H), 131.1 (*C*H), 130.1 (*C*H), 128.6 (*C*H), 128.4 (*C*), 128.2 (*C*H), 127.2 (*C*), 126.7 (*C*H), 61.3 ($SeCH_2$*C*HS), 16.7 (Se*C*H_2CHS) ppm.

$C_{14}H_{12}SOSe$: 307 g/mol.

8.5.3.2 (*S**,*S**)-2-Naphthyl-2,3-dihydro-1,4-benzoselenathiine-1-oxide (117)



Synthesised according to GP 4 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 34 mg 2-vinylnaphthalene (0.22 mmol) in tetrahydrofuran. After column chromatography (hexane/ethyl acetate, 4:1→1:1), the racemic product was in 16% yield (11 mg, 0.032 mmol) as colourless solid.

R_f (EA/Hex 1:1) = 0.50.

MS (ES+) m/z (%): 717 ($[2M+H]^+$, 55), 471 (10), 380 (10), 359 ($[M+H]^+$, 100).

HRMS (ES+): $[M+H]^+$ calculated for $C_{18}H_{15}OS^{80}Se$ 359.0003; found 359.0001.

IR (film): $\tilde{\nu}$ = 3055, 2926, 1443, 1425, 1051, 1031, 909, 856, 819, 751, 728 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.73–7.63 (m, 3H, Ar*H*), 7.55–7.50 (m, 2H, Ar*H*), 7.41–7.37 (m, 2H, Ar*H*), 7.30 (dt, *J* = 1.3 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.20–7.18 (m, 1H, Ar*H*), 7.18–7.13 (m, 1H, Ar*H*), 7.12–7.09 (m, 1H, Ar*H*), 4.61–4.56 (m, 1H, $SeCH_2CHS$), 3.92 (dd, *J* = 11.7 Hz, *J* = 8.4 Hz, 1H, SeCH*H*CHS), 3.31 (dd, *J* = 11.7 Hz, *J* = 6.03 Hz, 1H, SeC*H*HCHS) ppm.

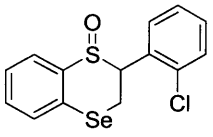
^{13}C NMR (125 MHz, $CDCl_3$): δ = 139.6 (*C*), 133.1 (*C*), 133.0 (*C*H), 132.3 (*C*H), 131.7 (*C*H), 131.1 (*C*H), 130.3 (*C*H), 128.2 (*C*H), 128.1 (*C*H), 127.7 (*C*H), 127.6 (*C*H), 127.3 (*C*), 126.7 (*C*H), 126.5 (*C*H), 126.4 (*C*H), 125.7 (*C*H), 61.5 ($SeCH_2$*C*HS), 16.8 (Se*C*H_2CHS) ppm.

^{77}Se NMR (57 MHz, $CDCl_3$): δ = 244 ppm.

M.P.: 114–116 °C.

$C_{18}H_{14}SOSe$: 357 g/mol.

8.5.3.3 (*S**,*S**)-2-(2-Chloro)phenyl-2,3-dihydro-1,4-benzselenathiine-1-oxide (118)



Synthesised according to GP 4 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 38 µl 2-chlorostyrene (0.30 mmol, 42 mg) in diethylether. After column chromatography (hexane/ethyl acetate, 4:1→1:1), the racemic product was in 9% yield (6 mg, 0.018 mmol) as colourless oil.

R_f (EA/Hex 1:3) = 0.10.

MS (ES+) m/z (%): 684 ($[2M+H]^+$, 14), 594 (30), 554 (10), 473 (20), 391 (32), 343 ($[M+H]^+$,100).

HRMS (ES+): $[M+H]^+$ calculated for $C_{14}H_{12}O^{35}ClS^{78}Se$ 342.9454; found 342.9457.

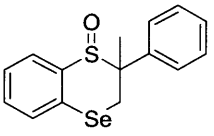
IR (film): $\tilde{\nu}$ = 3375, 3056, 2972, 2928, 1571, 1471, 1441, 1363, 1164, 1092, 1047, 755 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.67 (dd, *J* = 1.5 Hz, *J* = 7.7 Hz, 1H, Ar*H*), 7.55 (m, 1H, Ar*H*), 7.44–7.48 (m, 1H, Ar*H*), 7.41 (dd, *J* = 1.5 Hz, *J* = 7.7 Hz, 1H, Ar*H*), 7.27–7.36 (m, 4H, Ar*H*), 4.87 (dd, *J* = 3.7 Hz, *J* = 11.9 Hz, 1H, $SeCH_2CHS$), 4.10 (t, *J* = 11.9 Hz, 1H, SeC*H*HCHS), 3.10 (dd, *J* = 3.8 Hz, *J* = 11.9 Hz, 1H, SeCH*H*CHS) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.8 (*C*), 134.1 (*C*), 132.7 (2*C*H), 132.6 (*C*H), 130.8 (*C*H), 129.8 (*C*), 129.7 (*C*H), 128.8 (*C*H), 127.5 (*C*H), 127.3 (*C*), 126.0 (*C*H), 56.2 ($SeCH_2CHS$), 13.9 ($SeCH_2CHS$) ppm.

$C_{18}H_{14}SOSe$: 342 g/mol.

8.5.3.4 (*S**,*S**)-2-Methyl-2-phenyl-2,3-dihydro-1,4-benzselenathiine-1-oxide (119)



Synthesised according to GP 4 with 52 mg (0.1 mmol) *rac*-bis-[2-(*t*-butylsulfinyl)phenyl] diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), 54 mg silver triflate (0.21 mmol) and 39 µl α-methylstyrene (0.30 mmol, 35 mg) in dichloromethane. After column chromatography (hexane/ethyl acetate, 4:1→1:1) the racemic product was in 12% yield (8 mg, 0.024 mmol) as colourless oil.

R_f (EA/Hex 1:3) = 0.19.

MS (ES+): m/z (%): 645 ($[2M+H]^+$, 25), 490 (8), 338 (7), 323 ($[M+H]^+$, 100).

HRMS (ES+): calculated for $C_{15}H_{15}OS^{80}Se$ 323.0003; found 323.0002.

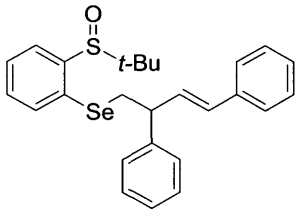
IR (film): $\tilde{\nu}$ = 3389, 2926, 1571, 1494, 1444, 1094, 1060, 755, 697 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (dd, *J* = 1.5 Hz, *J* = 7.7 Hz, 1H, Ar*H*), 7.69–7.65 (m, 2H, Ar*H*), 7.59 (dd, *J* = 1.1 Hz, *J* = 7.7 Hz, 1H, Ar*H*), 7.51–7.29 (m, 5H, Ar*H*), 3.58 (d, *J* = 12.3 Hz, 1H, SeC*H*HCS), 3.17 (d, *J* = 12.3 Hz, 1H, SeCH*H*CS), 1.46 (s, 3H, CH_3) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.2 (*C*), 131.7 (*C*H), 130.5 (*C*H), 128.9 (2*C*H), 128.4 (*C*H), 128.1 (*C*H), 127.6 (*C*), 127.5 (*C*H), 126.7 (*C*), 126.5 (2*C*H), 64.2 ($SeCH_2CS$), 30.6 (CH_3), 20.1 ($SeCH_2CS$) ppm.

$C_{15}H_{14}SOSe$: 321 g/mol.

8.5.3.5 *rac*-2-(*t*-Butylsulfinyl)phenyl-(*E*)-2,4-diphenylbut-3-enyl selenide (124)



rac-Bis[2-(*t*-butylsulfinyl)phenyl] diselenide (520 mg, 1.0 mmol) was dissolved in dry tetrahydrofuran (40 ml) under argon, cooled to –78 °C, and bromine (1.0 mmol, 1.0 ml of a 1 M solution in CCl_4) was added. After 20 min silver triflate (540 mg, 2.1 mmol) was added and the mixture was stirred for 25 min at –78 °C. Styrene (229 mg, 2.20 mmol) was added and the mixture warmed to –10 °C overnight. Then MeOH (1 ml) was added and the mixture was stirred for additional 60 min at 0 °C. The reaction mixture was quenched with aqueous saturated $NaHCO_3$ solution (1 ml) and water (40 ml). After extraction of the reaction mixture with dichloromethane (3 x 50 ml), drying of the combined organic phases with $MgSO_4$ and removal of the solvent under reduced pressure; the residue was purified by flash column chromatography on silica gel, yielding the addition products as pale yellow oils. The diastereomers could not be separated by flash chromatography (ethyl acetate/hexanes, 1:5); yield 30% (309 mg, 0.30 mmol), pale yellow grease, *d.r.*: 1:1.

R_f (EA/Hex 1:3) = 0.23.

MS (ES+) m/z (%): 969 ($[2M+H]^+$, 5), 937 (15), 501 (22), 469 ($[M+H]^+$, 100), 413 (27), 365 (5), 309 (7), 251(7), 207 (20).

HRMS (ES+): $[M+H]^+$ calculated for $C_{26}H_{29}OS^{74}Se$: 463.1158; found: 463.1163.

IR (film): $\tilde{\nu}$ = 3057, 3026, 2966, 2926, 1599, 1569, 1494, 1443, 1426, 1362, 1326, 1217, 1148, 1091, 965, 749, 699 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.73 (ddd, *J* = 1.4 Hz, *J* = 3.7 Hz, *J* = 7.8 Hz, 1H, Ar*H*), 7.45 (td, *J* = 1.2 Hz, J = 7.6 Hz, 1H, Ar*H*), 7.33–7.37 (m, 1H, Ar*H*), 7.16–7.24 (m, 11H, Ar*H*), 6.37 (dd, *J* = 15.9 Hz, *J* = 20.4 Hz, 1H, CH=C*H*Ar), 6.27 (ddd, *J* = 1.9 Hz, *J* = 7.6 Hz, *J* = 15.8 Hz, 1H, C*H*=CHAr), 3.69 (p, *J* = 7.4 Hz, 1H, $SeCH_2CH$), 3.30 (m, 2H, $SeCH_2CH$), 1.12 (s, 9H, $C(CH_3)_3$) ppm.

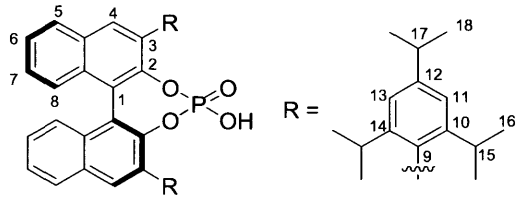
^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.4 (*C*), 143.4* (*C*), 142.7 (*C*), 142.6* (*C*), 136.9 (*C*), 136.8* (*C*), 133.7, 133.6*, 131.8, 131.8*, 131.7, 131.4, 131.4*, 131.1, 130.9, 128.7, 128.7*, 128.4, 127.6, 127.6*,

127.5, 127.4*, 127.0, 126.9*, 126.3, 126.3*, 122.5, 58.2 ($C(CH_3)_3$), 58.1* ($C(CH_3)_3$), 49.1 ($SeCH_2CH$), 49.0* ($SeCH_2CH$), 35.9 ($SeCH_2CH$), 35.8* ($SeCH_2CH$), 23.3 ($C(CH_3)_3$) ppm.

$C_{26}H_{28}SOSe$: 468 g/mol.

8.5.4 Chiral Counteranions

8.5.4.1 (*S*)-3,3'-Bis(2,4,6-triisopropylphenyl)-1,1'binaphthyl-2,2'-diyl hydrogen phosphate [(*S*)-153][141]



To a stirred solution of (*S*)-3,3'-bis(2,4,6-triisopropylphenyl)-2,2'-dihydroxy-1,1'-binaphthyl (690 mg, 1.00 mmol) in pyridine (2.0 ml), phosphorus oxychloride (160 µl, 1.75 mmol) was added dropwise, whereupon the temperature rose Complete dissolution was achieved by heating to 90 °C. The stirred solution was allowed to cool to 50–60 °C then water (120 µl) was added dropwise which increased the temperature to the boiling point (approx. 118 °C). The resulting solution was cooled to about 60 °C and added dropwise with vigorous stirring to 6 M HCl (3.0 ml), which gave a precipitate. The crude product was collected by suction filtration and the wet cake was once more stirred with 6 M HCl (2.0 ml). The suspension was heated to boiling and immediately cooled. The solid was thoroughly filtered by suction, washed twice with water (2 ml) and dried on high vacuum to afford 749 mg (0.99 mmol, 99%) product. The obtained spectroscopic data are in agreement with literature data.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 8.0 Hz, 2H, C*H*-5), 7.88 (s, 2H, C*H*-4), 7.53 (m, 2H, ArC*H*), 7.36 (m, 4H, ArC*H*), 7.14 (s, 1H, ArC*H*), 7.13 (s, 1H, ArC*H*), 7.03 (br s, 2H, C*H*-13), 2.98 (m, 2H, C*H*), 2.88 (m, 2H, C*H*), 2.67 (m, 2H, C*H*), 1.34 (dd, *J* = 3.0 Hz, *J* = 7.0 Hz, 6H, CH_3), 1.25 (dd, *J* = 3.0 Hz, *J* = 7.0 Hz, 12H, CH_3), 1.13 (d, *J* = 3.0 Hz, *J* = 7.0 Hz, 12H, CH_3), 0.96 (d, *J* = 7.0 Hz, 6H, CH_3) ppm.

^{31}P NMR (202 MHz, $CDCl_3$): δ = 3.1 ppm.

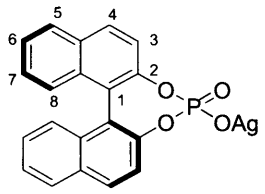
IR (KBr): $\tilde{\nu}$ = 2959, 2868, 1607, 1458, 1411, 1362, 1239, 1210, 1020, 997, 750 cm^{-1}.

M.P.: above 295°C

$[\alpha]_D^{20}$ = +73.4 (c = 0.1, $CHCl_3$).

$C_{50}H_{57}O_4P$: 753 g/mol.

8.5.4.2 (*S*)-(+)-1,1'-Binaphthyl-2,2-diyl silver phosphate [(*S*)-179]



To a solution of (*S*)-(+)-1,1'-binaphtyl-2,2-diyl hydrogen phosphate (132 mg, 0.380 mmol) in dichloromethane (2.8 ml) in the dark silver carbonate (52 mg, 0.19 mmol) was added in one portion, followed by distilled water (2.8 ml). The resulting mixture was stirred vigorously for 1 h. After this time, the mixture was diluted with dichloromethane (3 ml) and water (3 ml). The layers were separated and the aqueous layer extracted with dichloromethane (2 x 5 ml). The combined organic extracts were filtered through Celite and concentrated to afford the product as a white solid in 62% (107 mg, 0.236 mmol) yield.

^{1}H NMR (500 MHz, DMSO): δ = 8.08 (d, *J* = 8.0 Hz, 2H, C*H*-8), 8.03 (d, *J* = 8.0 Hz, 2H, C*H*-5), 7.49 (m, 4H, C*H*-4, C*H*-7), 7.32 (t, *J* = 8.0 Hz, 2H, C*H*-6), 7.22 (d, *J* = 8.0 Hz, 2H, C*H*-3) ppm.

^{13}C NMR (125 MHz, DMSO): δ = 149.8 (d, $J_{C\text{-}P}$ = 9 Hz, *C*-2), 131.9 (*C*-8a), 130.4 (*C*-4a), 129.9 (*C*H-4), 128.4 (*C*H-5), 126.1, 126.0, 124.5 (*C*H-6, *C*H-7, *C*H-8), 122.4 (*C*-1), 121.7 (*C*H-3) ppm.

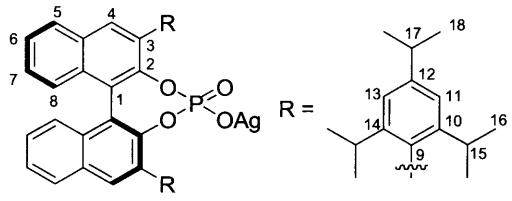
^{31}P NMR (202 MHz, DMSO): δ = 6.4 ppm.

MS (EI+) m/z (%): 455 (M+, 13), 428 (8), 349 (9), 186 (9), 128.5 (5), 107 (48), 80 (100).

IR (KBr): $\tilde{\nu}$ = 1241, 1216, 1098, 1068 cm^{-1}.

$C_{20}H_{12}AgO_4P$: 455 g/mol.

8.5.4.3 (*S*)-3,3'-Bis(2,4,6-triisopropylphenyl)-1,1'-binaphthyl-2,2'-diyl silver phosphate [(*S*)-180][103]



To a solution of (*S*)-3,3'-bis(2,4,6-triisopropylphenyl)-1,1'binaphthyl-2,2'-diyl hydrogen phosphate (301 mg, 0.40 mmol) in dichloromethane (3.0 ml), silver carbonate (56 mg, 0.20 mmol) was added in the dark in one portion, followed by distilled water (2.8 ml). The resulting mixture was stirred vigorously for 1 h. After this time, the mixture was diluted with dichloromethane (3 ml) and water (3 ml). The layers were separated and the aqueous layer extracted with dichloromethane (2 x 9 ml). The combined organic extracts were filtered through Celite and concentrated to afford the product as a

white solid in 45% yield (155 mg, 0.18 mmol). The obtained spectroscopic data are in agreement with literature data.

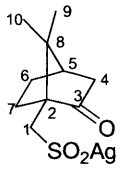
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.0 Hz, 2H, C*H*-5), 7.72 (br s, 2H C*H*-4), 7.38 (m, 2H, ArC*H*), 7.25 (m, 4H, ArC*H*), 7.05 (d, *J* = 7.0 Hz, 2H, ArC*H*), 6.90(br s, 2H, C*H*-13), 2.89 (m, 2H, C*H*), 2.79 (m, 2H, C*H*), 2.62 (m, 2H, C*H*), 1.24 (dd, *J* = 2.0 Hz, *J* = 7.0 Hz, 6H, CH_3), 1.18 (d, *J* = 7.0 Hz, 12H, CH_3), 0.95–0.15 (m, 12H, CH_3), 0.85 (d, *J* = 7.0 Hz, 6H, CH_3) ppm.

^{31}P NMR (202 MHz, DMSO): δ = 4.2 ppm.

IR (KBr): $\tilde{\nu}$ = 3057, 2957, 2867, 1601, 1462, 1412, 1361, 1239, 1206, 1151, 1084, 956, 873, 750 cm^{-1}.

$C_{50}H_{57}O_4PAg$: 860 g/mol.

8.5.4.4 Silver camphorsulfonate [(*S*)-182][121]

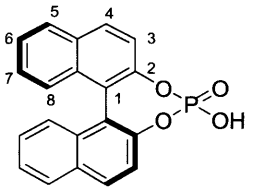


To a vigorously stirred suspension of silver oxide (277 mg, 1.2 mmol) in acetonitrile (1 ml), camphorsulfonic acid (232 mg, 1.00 mmol) in acetonitrile (1 ml) was added dropwise in the dark. After 30 min the excess of silver oxide was filtered off and the filtrate was evaporated to afford the product as a white solid in 73% (236 mg, 0.73 mmol) yield. The obtained spectroscopic data are in agreement with literature data.

^{1}H NMR (400 MHz, acetonitrile-d^3): 3.07 (d, *J* = 14.0 Hz, 1H, CH_2-1), 2.75 (m, 1H, CH_2-6), 2.59 (d, *J* = 14.0 Hz, 1H, CH_2-1), 2.20–2.32 (m, 1H, CH_2-4), 1.95–2.03 (m, 2H, C*H*-5, CH_2-7), 1.85 (d, *J* = 14.0 Hz, 1H, CH_2-4), 1.45–1.47 (m, 1H, CH_2-7), 1.36–1.37 (m, 1H, CH_2-6), 1.12 (s, 3H, CH_3), 0.83 (s, 3H, CH_3) ppm.

$C_{10}H_{15}SO_3Ag$: 323 g/mol.

8.5.4.5 (*S*)-(+)-1,1'-Binaphthyl-2,2-diyl hydrogen phosphate [(*S*)-185][113]



To a stirred solution of (*S*)-1,1'-bi-2,2'-naphthol (143 mg, 0.50 mmol) in pyridine (0.65 ml), phosphorus oxychloride (63 µl, 0.69 mmol) was added dropwise, whereupon the temperature rose. Complete dissolution was achieved by heating to 90 °C. The stirred solution was allowed to cool to

50–60 °C, then water (57 µl) was added dropwise which raised the temperature to the boiling point (approx. 118 °C). The resulting solution was cooled to about 60 °C and added dropwise with vigorous stirring to 6 M HCl (1.3 ml), which gave a precipitate. The crude product was collected by suction filtration and the wet cake was once more stirred with 6 M HCl (0.5 ml). The suspension was heated to boiling and immediately cooled. The solid was thoroughly filtered by suction, washed twice with 0.5 ml of water and dried on high vacuum to afford 147 mg (85%, 0.43 mmol) (*S*)-(+)-1,1'-binaphtyl-2,2-diyl hydrogen phosphate. The obtained spectroscopic data are in agreement with literature data.

^{1}H NMR (500 MHz, DMSO): δ = 8.18 (d, *J* = 8 Hz, 2H, C*H*-8), 8.09 (d , *J* = 8 Hz, 2H, C*H*-5), 7.57 (d, *J* = 9 Hz, 2H, C*H*-4), 7.52 (m, 2H, C*H*-7), 7.38 (t, *J* = 6 Hz, 2H, C*H*-6), 7.21 (d, *J* = 8 Hz, 2H, C*H*-3) ppm.

^{13}C NMR (125 MHz, DMSO): δ = 147.6 (d, $J_{C\text{-}P}$ = 10 Hz, *C*-2), 131.6 (*C*-8a), 131.0 (*C*-4, *C*-4a), 128.6 (C*H*-5), 126.8, 126.1, 125.5, 121.2 (C*H*-1), 121.0 (C*H*-3) ppm.

^{31}P NMR (202 MHz, DMSO): δ = 2.8 ppm.

MS (EI+) m/z (%): 348 (M^+, 12), 268 (12), 239(8), 83 (100).

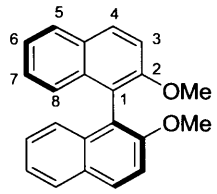
IR (KBr): $\tilde{\nu}$ = 1255, 1229, 1052 cm^{-1}.

M.P.: above 295°C

$[\alpha]_D^{20}$ = +697° (c = 0.1, MeOH).

$C_{20}H_{13}O_4P$: 348 g/mol

8.5.4.6 (*S*)-2,2'-Dimethoxy-1,1'-binaphthyl [(*S*)-186][114]



To a suspension of (*S*)-1,1'-bi-2,2'-naphthol (2.50 mmol, 716 mg) and potassium carbonate (8.25 mmol, 1.14 g) in acetone (30 ml), methyl iodide (7.50 mmol, 467µl) was added and the mixture was heated at reflux for 24 h. Additional methyl iodide (2.50 mmol, 156 µl) was added and heating continued for 12 h. Three quarters of the solvent were evaporated and the residue was treated with water (20 ml). The suspension was further stirred for 8 h and then filtrated by suction, washed twice with water (10 ml) and dried on high vacuum to afford (*S*)-2,2'-dimethoxy-1,1'-binaphthyl as colourless crystals in quantitative yield (785 mg, 2.5 mmol). The obtained spectroscopic data are in agreement with literature data.

R_f (EA/Hex 1:1) = 0.48.

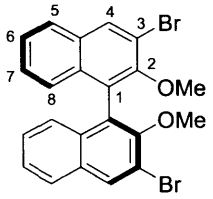
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 9.0 Hz, 2H, C*H*-5), 7.79 (d , *J* = 8.0 Hz, 2H, C*H*-8), 7.41 (d, *J* = 9.0 Hz, 2H, C*H*-4), 7.23 (t, *J* = 8.0 Hz, 2H, C*H*-6 or C*H*-7), 7.12 (t, *J* = 8.0 Hz, 2H, C*H*-6 or C*H*-7), 7.01 (d, *J* = 9.0 Hz, 2H, C*H*-3), 3.69 (s, 6H, OCH_3) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.1 (*C*-2), 134.1(*C*-8a), 129.4 (*C*H-4), 129.3 (*C*-4a), 127.9 (*C*H-5), 126.3, 125.3, 123.5 (*C*H-6, *C*H-7, *C*H-8), 119.8 (*C*H-1), 114.4 (*C*H-3), 57.0 (OCH_3) ppm.

M.P.: 194–195°C.

$C_{22}H_{18}O_2$: 314 g/mol.

8.5.4.7 (*S*)-3,3′-Dibromo-2,2'-dimethoxy-1,1'-binaphthyl [(*S*)-187][114]



To a solution of tetramethylethylendiamine (TMEDA; 17.64 mmol, 2.70 ml) in dry diethyl ether (130 ml), *n*-butyllithium (19.3 mmol, 2.5 M solution in hexane, 7.72 ml) was added at room temperature. The mixture was stirred for 15 min at this temperature, then (*S*)-2,2'-dimethoxy-1,1'-binaphthyl (8.40 mmol, 2.65 g) was added in one portion. The white suspension turned light brown during stirring at room temperature for 4 h. The mixture was then cooled to –78 °C and bromine (17 mmol, 0.89 ml) was added slowly. The mixture was stirred overnight and the temperature was allowed to rise to –50 °C. The suspension was stirred additional 4 h at room temperature. Then a saturated aqueous solution of sodium sulfite (60 ml) was added and the mixture was stirred additional 4 h. The layers were separated and the aqueous layer was extracted with dichloromethane (3 x 70 ml). The combined organic layers were dried with Na_2SO_4, filtrated and the solvent was removed in vacuo. After silica gel chromatography (petroleum ether), (*S*)-3,3′-dibromo-2,2'-dimethoxy-1,1'-binaphthyl was obtained as a colourless solid in 50% yield (1.98 g, 4.20 mmol). The obtained spectroscopic data are in agreement with literature data.

R_f (EA/Hex 1:1) = 0.65.

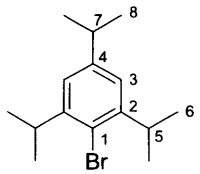
^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.29 (s, 2H, C*H*-4), 7.83 (d, *J* = 8.0 Hz, 2H, C*H*-5), 7.44 (t, *J* = 4 Hz, 2H, C*H*-6), 7.28 (t, *J* = 4.0 Hz, 2H, C*H*-7), 7.09 (d, *J* = 8.0 Hz, 2H, C*H*-8), 3.51 (s, 6 H, OCH_3) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.9 (*C*-2), 133.5 (*C*-8a), 133.4 (*C*H-4), 131.9 (*C*-4a), 127.6, 127.3 (*C*H-5, *C*H-7), 127.0 (*C*H-1), 126.3, 126.2 (*C*H-6, *C*H-8), 117.9 (*C*H-3), 61.5 (OCH_3) ppm.

$[\alpha]_D^{20}$ = –70.3 (c = 0.11, THF).

$C_{22}H_{16}Br_2O_2$: 472 g/mol.

8.5.4.8 2-Bromo-1,3,5-triisopropylbenzene (189)[116]



An ice cold solution of Br_2 (2.05 ml, 6.46g, 40.0 mmol) in dimethylformamide (6 ml) (prepared by slowly adding Br_2 to stirred, chilled dimethylformamide) was added to a stirred light protected solution of 1,3,5-triisopropylbenzene (2.42 ml, 2.04 g, 10.0 mmol) in dimethylformamide (8 ml) at 0 °C. Stirring was continued for 20 min at this temperature. Then the mixture was poured into an ice cold mixture of sodium sulfite (4 g) and water (20 g). The oil was extracted into hexane, the combined organic layers were dried with Na_2SO_4 and the solvent was evaporated. The crude, pure product was obtained in 92% yield (2.60 g, 9.20 mmol) as colourless liquid. The obtained spectroscopic data are in agreement with literature data.

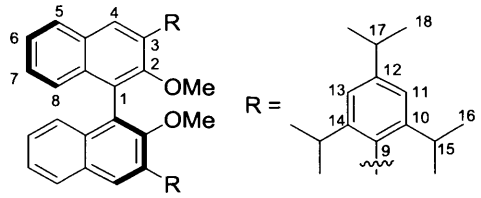
R_f (E/PE 1:1) = 0.67.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.90 (s, 2H, C*H*-3), 3.39 (m, 2H, C*H*-5), 2.78 (m, 1H, C*H*-7), 1.15 (d, *J* = 10 Hz, 18H, CH_3-6 and CH_3-8) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.8 (*C*-4), 147.4 (*C*-2), 123.6 (*C*H-3), 122.3 (C-1), 34.1 (*C*H-7), 33.6 (*C*H-5), 24.1 (*C*H_3-8), 23.3 (*C*H_3-6) ppm.

$C_{15}H_{23}Br$: 283 g/mol.

8.5.4.9 (*S*)-3,3'-Bis(2,4,6-triisopropylphenyl)-2,2'-dimethoxy-1,1'binaphthyl [(*S*)-191][115]



(*S*)-3,3'-Dibromo-2,2'-dimethoxy-1,1'binaphthyl (3.39 mmol, 1.60 g) and $Ni(PPh_3)_2Cl_2$ (0.67 mmol, 443 mg) were suspended in dry diethyl ether (40 ml). To this suspension was slowly added freshly prepared (2,4,6-triisopropylphenyl)magnesium bromide (synthesis see 8.5.1.20) (0.56 M solution in THF, 18.2 ml, 10.2 mmol) at room temperature. The mixture was allowed to stir at this temperature until it got dark green (approx. 10 min), at this point it was refluxed for 24 h. Then it was cooled to 0 °C and quenched with 1 M HCl until neutral. The layers were separated and the aqueous layer was washed with diethyl ether (3 x 75 ml). The combined organic layers were dried with $MgSO_4$, filtrated and the solvent was removed under reduced pressure. The crude solid product was purified by silica gel chromatography (petroleum ether). 2.00 g (82%, 2.78 mmol) of still slightly contaminated product

was obtained as a light brown solid. The obtained spectroscopic data are in agreement with literature data.

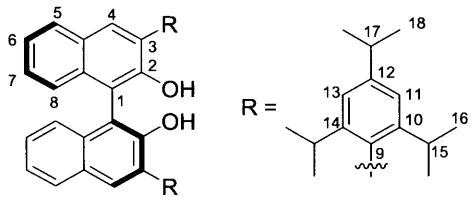
R_f (EA/Hex 1:6) = 0.67.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 9.0 Hz, 2H, C*H*-5), 7.66 (s, 2H, C*H*-4), 7.33 (m, 2H, Ar*H*), 7.24 (m, 2H, Ar*H*), 7.01 (d, *J* = 6.0 Hz, 4H, Ar*H*), 3.00 (s, 6H, OCH_3), 2.88 (m, 2H, C*H*), 2.77 (m, 2H, C*H*), 2.71 (m, 2H, C*H*), 1.24 (d, *J* = 7.0 Hz, 12H, CH_3), 1.12 (d, *J* = 7.0 Hz, 6H, CH_3), 1.09 (d, *J* = 7.0 Hz, 6H, CH_3) 1.05 (d, *J* = 7.0 Hz, 6H, CH_3) 1.00 (d, *J* = 7.0 Hz, 6H, CH_3) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.1 (*C*-2), 148.1, 147.0, 146.7 (*C*-10, *C*-12, *C*-14), 134.1 (Ar*C*), 133.9 (Ar*C*), 133.3 (Ar*C*), 130.9 (*C*H-4), 130.2 (Ar*C*), 127.9, 125.9, 125.8 (*C*H-5, *C*H-7, *C*H-8), 124.7 (*C*-1), 124.5 (*C*H-6), 120.6 (*C*H-11, *C*H-13), 59.8 (O*C*H_3), 34.3 (*C*H), 31.0 (*C*H), 30.8 (*C*H), 25.5 (*C*H_3), 25.3 (*C*H_3), 24.2 (*C*H_3), 24.1 (*C*H_3), 23.4 (*C*H_3), 23.3 (*C*H_3) ppm.

$C_{52}H_{62}O_2$: 719 g/mol.

8.5.4.10 (*S*)-3,3'-Bis(2,4,6-triisopropylphenyl)-2,2'-dihydroxy-1,1'binaphthyl [(*S*)-192][115]



To a solution of (*S*)-3,3'-bis(2,4,6-triisopropylphenyl)-2,2'-dimethoxy-1,1'dinaphthyl (2.00 g, 2.78 mmol) in dichloromethane (75 ml), a BBr_3-solution (10 ml, 1 M in dichloromethane) was added slowly at 0 °C. The resulting mixture was allowed to warm to room temperature overnight. The mixture was then cooled again to 0 °C and the reaction was quenched by the slow addition of water (30 ml). The layers were separated and the aqueous layer was extracted with dichloromethane (3 x 30 ml). The combined organic layers were dried with $MgSO_4$ and filtrated. The solvent was removed under reduced pressure and the crude solid product was purified by chromatography (petroleum ether). 1.90 g (99%, 2.75 mmol) of still slightly contaminated product was obtained as a light brown solid. The obtained spectroscopic data are in agreement with literature data.

R_f (EA/Hex 1:6) = 0.62.

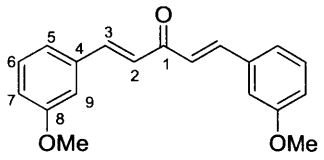
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.0 Hz, 2H, C*H*-5), 7.79 (s, 2H, C*H*-4), 7.40 (ddd, *J* = 2.0 Hz, *J* = 6.0 Hz, *J* = 8.0 Hz, 2H, ArC*H*), 7.29–7.36 (m, 4H, ArC*H*), 7.15 (dd, *J* = 2.0 Hz, *J* = 8.0 Hz, 4H, C*H*-11 and C*H*-13), 4.94 (br s, 2H, O*H*), 3.97–3.99 (m, 2H, C*H*), 2.86–2.88 (m, 2H, C*H*), 2.70–2.72 (m, 2H, C*H*), 1.34 (d, *J* = 7.0 Hz, 12H, CH_3), 1.22 (d, *J* = 7.0 Hz, 6H, CH_3), 1.13 (d, *J* = 7.0 Hz, 6H, CH_3) 1.11 (d, *J* = 7.0 Hz, 6H, CH_3) 1.05 (d, *J* = 7.1 Hz, 6H, CH_3) ppm.

IR (KBr): $\tilde{\nu}$ = 3052, 2958, 2880, 1603, 1498, 1457, 1423, 1382, 1362, 1255, 1233, 1147, 750 cm^{-1}.

$[\alpha]_D^{20}$ = –84.3 (c = 0.12, THF).

$C_{50}H_{58}O_2$: 690 g/mol.

8.5.4.11 (1*E*,4*E*)-1,5-Bis(3-methoxyphenyl)penta-1,4-dien-3-one (194)[118]



A solution of freshly distilled *m*-anisaldehyde (40 mmol, 5.5 g) and acetone (20 mmol, 1.46 ml) in ethanol (6 ml) was added dropwise to a stirred solution of sodium hydroxide (4 g) in 50% aqueous ethanol (72 ml) at room temperature. After 2 h, the mixture was diluted with dichloromethane (100 ml), washed with water (100 ml) and dried over Na_2SO_4. After filtration, the crude title compound was obtained as a yellow wax in 60% yield (3.53 g, 12 mmol). The obtained spectroscopic data are in agreement with literature data.

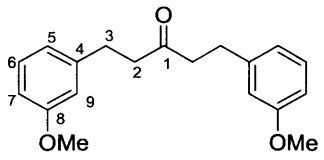
R_f (EA/Hex 1:1) = 0.58.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 16.0 Hz, 2H, C*H*-3), 7.35 (t, *J* = 8.0 Hz, 2H, C*H*-6), 7.22 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.15 (m, 2H, Ar*H*), 7.11 (d, *J* = 16.0 Hz, 2H, C*H*-2), 6.99 (m, 2H, Ar*H*), 3.89 (s, 6H, OC*H*$_3$) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.2 (*C*-1), 160.3 (*C*-8), 143.7 (C*H*-3), 136.6 (*C*-4), 130.3, 126.0, 121.5, 116.8, 113.7, 55.7 (O*C*H$_3$) ppm.

$C_{19}H_{18}O_3$: 294 g/mol.

8.5.4.12 1,5-Bis(3-methoxyphenyl)pentan-3-one (195)[118]



A solution of crude (1*E*,4*E*)-1,5-bis(3-methoxyphenyl)penta-1,4-dien-3-one (1.53 mmol, 450 mg) in acetone (9 ml) was stirred with Raney-Ni (~1.5 g, 50% in water) under an atmosphere of hydrogen at room temperature. The reaction progress was monitored by TLC. When the starting material had disappeared (~24 h), the catalyst was filtered off and washed with acetone/water (3:1). The filtrate was evaporated and the residue extracted with dichloromethane (3 x 6 ml). The combined organic layers were dried with Na_2SO_4 and the solvent was removed in vacuo. After column chromatography (hexane/ethyl acetate 10:1) the product was obtained as colourless oil in 89% yield (406 mg, 1.36 mmol). The obtained spectroscopic data are in agreement with literature data.

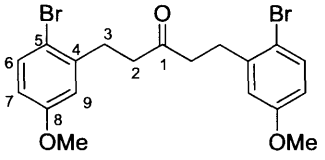
R_f (EA/Hex 1:6) = 0.28.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.09 (t, *J* = 8.0 Hz, 2H, C*H*-6), 6.59–6.65 (m, 6H, Ar*H*), 3.68 (s, 6H, OCH_3), 2.77 (t, *J* = 7.5 Hz, 4H, CH_2-3), 2.60 (t, *J* = 7.5 Hz, 4H, CH_2-2) ppm.

^{13}C NMR (63 MHz, $CDCl_3$): δ = 209.0 (*C*-1), 159.8 (*C*-8), 142.7 (*C*-4), 129.5, 120.7 (*C*H-5, *C*H-6), 114.1, 111.4 (*C*H-7, *C*H-9), 55.2 (O*C*H_3), 44.4 (*C*H_2-2), 29.8 (*C*H_2-3) ppm.

$C_{19}H_{22}O_3$: 298 g/mol.

8.5.4.13 1,5-Bis-(2-bromo-5-methoxyphenyl)pentan-3-one (196) [118]



To a solution of 1,5-bis-(3-methoxyphenyl)pentan-3-one (1.00 mmol, 296 mg) in dichloromethane (10 ml), pyridine (3.5 mmol, 283 µl) was added, and the mixture was cooled to –10 °C. A solution of bromine in dichloromethane (10% v/v, 2.5 mmol, 1.3 ml) was added dropwise. After the addition was complete, the reaction mixture was allowed to warm to room temperature and stirred until the starting material had disappeared (~18 h). The mixture was quenched with 10% aqueous sodium bisulfite solution (10 ml) and stirred for additional 15 min. The layers were separated and the organic layer was washed with 1 M hydrochloric acid (10 ml), water (10 ml) and brine (10 ml). The organic layer was dried with Na_2SO_4 and the solvent was removed under reduced pressure. The product was obtained as light yellow oil in 85% yield (388 mg, 0.85 mmol). The obtained spectroscopic data are in agreement with literature data.

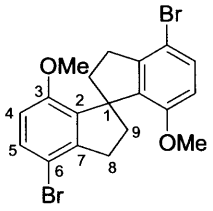
R_f (EA/Hex 1:6) = 0.28.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31 (d, *J* = 9.0 Hz, 2H, Ar*H*), 6.71 (d, *J* = 4.0 Hz, 2H, Ar*H*), 6.57 (dd, *J* = 4.0 Hz, *J* = 9.0 Hz, 2H, Ar*H*), 3.70 (s, 6H, OCH_3), 2.78 (t, *J* = 8.0 Hz, 4H, CH_2-3), 2.65 (t, *J* = 8.0 Hz, 4H, CH_2-2) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 208.4 (*C*-1), 159.0 (*C*-8), 141.2 (*C*-4), 133.4 (*C*-5), 116.2, 114.6, 113.6 (*C*-6, *C*-7, *C*-9), 55.4 (O*C*H_3), 42.5 (*C*H_2-2), 29.3 (*C*H_2-3) ppm.

$C_{19}H_{20}Br_2O_3$: 456 g/mol.

8.5.4.14 *rac*-4,4'-Dibromo-7,7'-dimethoxy-1,1'-spirobiindane (197) [118]



1,5-Bis-(2-bromo-5-methoxyphenyl)-3-pentanone (7.80 mmol, 3.50 g) was stirred with polyphosphoric acid (30 g) at 105 °C for 6 h. After cooling to room temperature, the mixture was quenched with ice-water (300 ml) and extracted with diethyl ether (2 x 300 ml), then with dichloromethane (4 x 300 ml). The combined extracts were dried with $MgSO_4$ and evaporated. 2.54 g (5.80 mmol) of crude crystalline 4,4'-dibromo-7,7'-dimethoxy-1,1'-spirobiindane were obtained. The obtained spectroscopic data are in agreement with literature data.[19]

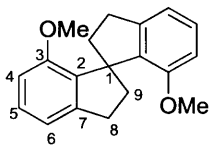
R_f (EA/Hex 1:3) = 0.39.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 9.0 Hz, 2H, C*H*-5), 6.52 (d, *J* = 9.0 Hz, 2H, C*H*-4), 3.52 (s, 6H, OC*H*$_3$), 3.05 (m, 2H, C*H*$_2$-8), 2.96 (m, 2H, C*H*$_2$-8), 2.31 (m, 2H, C*H*$_2$-9), 2.16 (m, 2H, C*H*$_2$-9) ppm.

^{13}C NMR (63 MHz, $CDCl_3$): δ = 155.7 (*C*-3), 144.9 (*C*-7), 138.0 (*C*-2), 130.4 (*C*-5), 110.9 (*C*-4), 110.6 (*C*-6), 60.4 (*C*-1), 55.4 (OCH_3), 38.0, 33.2 (*C*-8, *C*-9) ppm.

$C_{19}H_{18}Br_2O_2$: 438 g/mol.

8.5.4.15 *rac*-7,7'-Dimethoxy-1,1'-spirobiindane (198) [118]



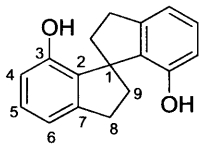
Crude *rac*-4,4'-dibromo-7,7'-dimethoxy-1,1'-spirobiindane (5.80 mmol, 2.54 g) was dissolved in dry THF (50 ml) and cooled to –78 °C with argon atmosphere and 4 equivalents of *n*-butyllithium (5.63 ml, 14.1 mmol, 2 M solution in hexanes) were added dropwise. After 1 h, the reaction was quenched by addition of ethanol (2.5 ml). The mixture was diluted with dichloromethane and water and the layers were separated. The aqueous layer was extracted with dichloromethane (2 x 30 ml) and the combined organic layers were dried with Na_2SO_4. 1.71 g of crude *rac*-7,7'-dimethoxy-1,1'-spirobiindane were obtained as yellow solid. The obtained spectroscopic data are in agreement with literature data.

R_f (EA/Hex 1:3) = 0.51.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.16 (t, *J* = 8.0 Hz, 2H, C*H*-5), 6.90 (d, *J* = 8.0 Hz, 2H, C*H*-6), 6.65 (d, *J* = 8.0 Hz, 2H C*H*-4), 3.55 (s, 6H, OCH_3), 3.00–3.15 (m, 4H, CH_2-8), 2.35–2.40 (m, 2H, CH_2-9), 2.15–2.25 (m, 2H, CH_2-9) ppm.

$C_{19}H_{20}O_2$: 280 g/mol.

8.5.4.16 *rac*-1,1'-Spirobiindane-7,7'-diol (199)[118]



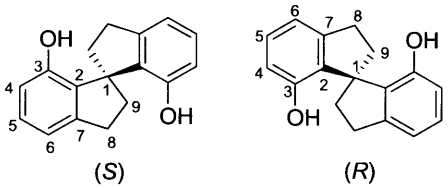
In a flame-dried flask under an argon atmosphere, a solution of *rac*-7,7'-dimethoxy-1,1'-spirobiindane (1.71 g) in dry dichloromethane (26 ml) was cooled to –78°C and 2.3 equivalents of BBr_3 (13.34 ml, 13.34 mmol, 1M solution in dichloromethane) were added dropwise to the mixture. After the addition was complete, the mixture was allowed to warm to room temperature overnight. The mixture was diluted with dichloromethane (100 ml) and washed with water (100 ml) until the washings were neutral. The solution was dried over Na_2SO_4 and the solvent was removed under reduced pressure to give 420 mg (1.66 mmol) of *rac*-1,1'-spirobiindane-7,7'-diol (21 % yield over 3 steps). The obtained spectroscopic data are in agreement with literature data.

R_f (EA/Hex 1:3) = 0.35.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17 (t, *J* = 8.0 Hz, 2H, C*H*-5), 6.89 (d, *J* = 8.0 Hz, 2H, C*H*-6), 6.68 (d, *J* = 8.0 Hz, 2H, C*H*-4), 4.61 (br s, 2H, O*H*), 2.95–3.15 (m, 4H, CH_2-8), 2.29–2.35 (m, 2H, CH_2-9), 2.19–2.18 (m, 2H, CH_2-9) ppm.

$C_{17}H_{16}O_2$: 252 g/mol.

8.5.4.17 (*S*)-(–)- and (*R*)-(+)-1,1'-Spirobiindane-7,7'-diol (199)[118]



(*S*)-(–)-1,1'-Spirobiindane-7,7'-diol [(*S*)-199]: Synthesised according to GP 5 with (0.55 mmol) (*S*)-7,7'-bis-(*L*-menthyloxy-carbonyloxy)-1,1'-spirobiindane. After column chromatography (hexane/ethyl acetate, 1:1) the product was isolated in 75% yield (105.0 mg, 0.413 mmol) as colourless solid. The obtained spectroscopic data are in agreement with literature data.

R_f (EA/Hex 1:3) = 0.35.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.02 (t, *J* = 8.0 Hz, 2H, C*H*-5), 6.75 (d, *J* = 8.0 Hz, 2H, C*H*-6), 6.54 (d, *J* = 8.0 Hz, 2H, C*H*-4), 4.70 (br s, 2H, O*H*), 2.90 (m, 4H, CH_2-8), 2.05–2.20 (m, 4H, CH_2-9) ppm.

$[\alpha]_{20}^{D}$ = –30.2 (c = 0.1, CH_2Cl_2).

$C_{17}H_{16}O_2$: 252 g/mol.

(*R*)-(+)-1,1'-Spirobiindane-7,7'-diol [(*S*)-199]: Synthesised according to GP 5 with (0.72 mmol) (*R*)-7,7'-bis-(*L*-menthyloxy-carbonyloxy)-1,1'-spirobiindane. After column chromatography (hexane/ethyl acetate, 1:1) the product was isolated in 83% yield (150.0 mg, 0.598 mmol) as colourless solid. The obtained spectroscopic data are in agreement with literature data.[19]

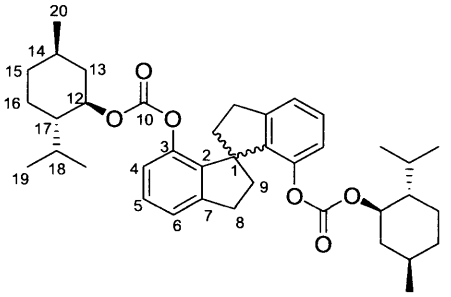
R_f (EA/Hex 1:3) = 0.35.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.04 (t, *J* = 8.0 Hz, 2H, C*H*-5), 6.77 (d, *J* = 7.0 Hz, 2H, C*H*-6), 6.54 (d, *J* = 8.0 Hz, 2H, C*H*-4), 4.72 (br s, 2H, O*H*), 2.91 (m, 4H, CH_2-8), 2.01–2.10 (m, 4H, CH_2-9) ppm.

$[\alpha]_{20}^{D}$ = +31.0 (c = 0.1, CH_2Cl_2).

$C_{17}H_{16}O_2$: 252 g/mol.

8.5.4.18 7,7'-Bis-(*L*-menthyloxy-carbonyloxy)- 1,1'-spirobiindane (201) [118]



L-Menthyl chloroformate (4.30 mmol, 849 µl) was added to a stirring solution of *rac*-1,1'-spirobiindane-7,7'-diol (1.67 mmol, 420 mg), triethylamine (6.16 mmol, 855 µl), and dimethylaminopyridine (DMAP, 0.17 mmol, 21 mg) in dichloromethane (7 ml) under argon. After stirring overnight, the mixture was washed with water (10 ml), 1 M HCl (10 ml) and brine (10 ml). The organic layer was dried with Na_2SO_4 and the solvent removed under reduced pressure. The diastereomers were separated by chromatography (diethyl ether/hexane 3:97). The obtained spectroscopic data are in agreement with literature data.

The diastereomer (*R*)-7,7'-bis-(*L*-menthyloxy-carbonyloxy)-1,1'-spirobiindane **(201a)** was isolated in 43% yield (425 mg, 0.718 mmol) as colourless oil.

R_f (E/Hex 10:1) = 0.25.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.11 (t, *J* = 7.0 Hz, 2H, C*H*-5), 7.00 (d, *J* = 7.0 Hz, 2H, Ar*H*), 6.89 (d, *J* = 8.0 Hz, 2H, Ar*H*), 4.22 (ddd, *J* = 4.0 Hz, *J* = 7.0 Hz, *J* = 11.0 Hz, 2H, C*H*-12), 2.95–2.99 (m,

4H, CH_2-8), 2.26–2.29 (m, 2H, CH_2-9), 2.17–2.19 (m, 2H, CH_2-9), 1.79 (br d, 2H, CH_2), 1.67–1.71 (m, 2H, C*H*), 1.52–1.56 (m, 4H, CH_2), 1.30–1.33 (m, 2H C*H*), 1.17–1.20 (m, 4H, CH_2), 0.87–0.90 (m, 2 H, CH_2), 0.82 (d, J = 7.0 Hz, 6H, CH_3), 0.71–0.76 (m, 8 H, C*H*, CH_3), 0.61 (d, J = 7 Hz, 6H, CH_3) ppm.

The diastereomer (*S*)-7,7'-bis-(*L*-menthyloxy-carbonyloxy)-1,1'-spirobiindane **(201b)** was isolated in 33% yield (325 mg, 0.551 mmol) as colourless solid.

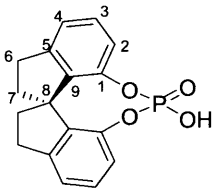
R_f (E/Hex 10:1) = 0.18.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.12 (t, J = 7.0 Hz, 2H, C*H*-5), 7.03 (d, J = 7.0 Hz, 2H, Ar*H*), 6.85 (d, J = 8.0 Hz, 2H, Ar*H*), 4.28 (dt, J = 4.0 Hz, J = 7.0 Hz, J = 11.0 Hz, 2H, C*H*-12), 2.90–2.93 (m, 4 H, CH_2-8), 2.19 (ddd, J = 2.0 Hz, J = 7.0 Hz, J = 13.0 Hz, 2H, CH_2-9), 2.06–2.09 (m, 2 H, CH_2-9), 1.81 (br d, 2H, CH_2), 1.52–1.56 (m, 4 H, CH_2), 1.43 (dtd, J = 2.0 Hz, J = 7.0 Hz, J = 14.0 Hz, 2H, C*H*), 1.28–1.31 (m, 2H, C*H*), 1.10–1.18 (m, 4H, CH_2), 0.87–0.89 (m, 2 H, CH_2), 0.81 (d, J = 7.0 Hz, 6H, CH_3), 0.73–0.78 (m, 8 H, C*H*, CH_3), 0.60 (d, J = 7.0 Hz, 6H, CH_3) ppm.

^{13}C NMR (63 MHz, $CDCl_3$): δ = 153.3 (*C*-10), 147.6 (*C*-3), 145.6 (*C*-7), 139.2 (*C*-2), 128.0, 122.2, 120.5 (*C*H-4, *C*H-5, *C*H-6), 78.6, 59.0 (*C*-1), 46.8, 40.5, 38.5, 34.1, 31.3, 31.1, 25.6, 23.1, 22.0, 20.8, 16.1 (*C*H$_3$) ppm.

$C_{41}H_{56}O_4$: 613 g/mol.

8.5.4.19 (*S*)-(–)-1,1'-Spirobiindane-7,7'-diyl hydrogen phosphate [(*S*)-202]



To a stirred solution of (*S*)-(–)-1,1'-spirobiindane-7,7'-diol (105 mg, 0.420 mmol) in pyridine (0.6 ml) was added phosphorus oxychloride (68 µl, 0.74 mmol) dropwise, whereupon the temperature rose. The mixture was further heated to 90 °C for 10 min. The stirred cloudy mixture was allowed to cool to 50-60 °C then water (40 µl) was added dropwise and the temperature of the mixture increased. It was further heated to 120 °C for 5 min and the resulting solution was then cooled to about 60 °C and pyridine (0.2 ml) was added. 6 M HCl (0.6 ml) was added dropwise with vigorous stirring, which produced a precipitate. The crude product was collected by suction filtration and the wet cake was once more stirred with 6 M HCl (0.4 ml). The suspension was heated to boiling and immediately cooled. The solid was thoroughly filtered by suction, washed twice with water (0.5 ml) and dried under high vacuum to afford 50 mg (38%, 0.16 mmol) of (*S*)-(–)-1,1'-spirobiindane-7,7'-diylhydrogen phosphate.

^{1}H NMR (400 MHz, $CHCl_3$): δ = 7.95 (br s, 1H, PO*H*), 7.19–7.23 (m, 2H, Ar*H*) 7.14 (t, *J* = 6.0 Hz, 2H, C*H*-3), 7.08 (d, *J* = 8.0 Hz, 1H, Ar*H*), 6.95 (d, *J* = 8.0 Hz, 1H, Ar*H*), 3.00–3.10 (m, 2H, CH_2), 2.75–2.85 (m, 2H, CH_2), 2.22 (t, *J* = 6 Hz, 2H, CH_2), 1.96–1.98 (m, 2H, CH_2) ppm.

^{13}C NMR (126 MHz, $CHCl_3$): δ = 146.9 (d, $J_{C\text{-}P}$ = 35 Hz, *C*-1), 144.4 (d, $J_{C\text{-}P}$ = 9 Hz, $J_{C\text{-}P}$ = 240 Hz, *C*-5), 138.9 (d, $J_{C\text{-}P}$ = 4 Hz, $J_{C\text{-}P}$ = 17 Hz, *C*-9), 129.0 (d, $J_{C\text{-}P}$ = 2 Hz, $J_{C\text{-}P}$ = 52 Hz, *C*H-3), 123.7 (d, $J_{C\text{-}P}$ = 2 Hz, $J_{C\text{-}P}$ = 35 Hz, *C*H-4), 121.3 (d, $J_{C\text{-}P}$ = 4 Hz, $J_{C\text{-}P}$ = 52 Hz, *C*H-2), 59.4 (*C*-8), 38.3 (*C*H_2-7), 30.4 (d, $J_{C\text{-}P}$ = 11 Hz, *C*H_2-6) ppm.

^{31}P NMR (202 MHz, $CHCl_3$): δ = –7.6 ppm.

IR (KBr): $\tilde{\nu}$ = 3850, 2946, 1616, 1581, 1463, 1309, 1219, 1154, 1131, 1064, 1018, 999, 928, 907, 856, 787, 635 cm^{-1}.

MS (EI+) m/z (%): 350 (78), 333 ($[M+NH_4]^+$, 100), 148 (5), 111 (8), 72 (13), 60 (20), 54 (27).

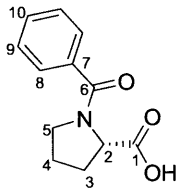
HRMS (ES+): $[M+H]^+$ calculated for $C_{17}H_{16}O_4{}^{31}P$: 313.0635; found 313.0633.

M.P.: Degradation above 270 °C.

$[\alpha]_{20}^{D}$ = –153 (c = 0.1, CH_2Cl_2).

$C_{17}H_{15}O_4P$: 314 g/mol.

8.5.4.20 *N*-Benzoylproline [(*S*)-205][120]



L-Proline (1.15 g, 10.0 mmol) was dissolved in 2 M NaOH (15 ml) at 0 °C and treated with benzoyl chloride (1.3 ml, 11 mmol) at the same temperature. The solution was vigorously stirred and cooled throughout, and it was kept alkaline by addition of more alkali if necessary. After 30 min the solution was acidified with 1 M HCl (30 ml). The aqueous layer was extracted three times with dichloromethane (30 ml); the organic layers were combined, dried with anhydrous Na_2SO_4, and then concentrated under reduced pressure. The residue was purified by column chromatography (hexane/ethyl acetate 2:1, 1:4), to give the product as colourless needles (1.36 g, 6.20 mmol, 62% yield). The obtained spectroscopic data are in agreement with literature data.

R_f (EA/Hex 1:3) = 0.10.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49 (dd, *J* = 1.4 Hz, *J* = 6.4 Hz, 2H, Ar*H*), 7.30–7.33 (m, 3H, Ar*H*), 4.64 (dd, *J* = 5.6 Hz, *J* = 8.1 Hz, 1H, C*H*-2), 3.51 (td, *J* = 7.0 Hz, *J* = 13.9 Hz, 1H, CH_2-5), 3.40–3.42

(m, 1H, CH_2-5), 2.21–2.23 (m, 1H CH_2-3), 2.01 (td, J = 6.2 Hz, J = 13.8 Hz, 1H, CH_2-3), 1.88–1.90 (m, 1H, CH_2-4), 1.75–1.77 (m, 1H, CH_2-4) ppm.

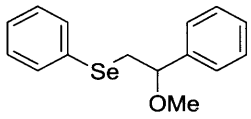
^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.7 (*C*-6), 171.1 (*C*-1), 135.4 (*C*-7), 130.6 (*C*H-10), 128.4, 127.3 (*C*H-8, *C*H-9), 59.7 (*C*H-2), 50.4 (*C*H_2-5), 28.7 (*C*H_2-3), 25.2 (*C*H_2-4) ppm.

M.P.: 153–154°C.

$[\alpha]_D^{20}$ = –95.2 (c = 0.12, MeOH).

$C_{12}H_{13}NO_3$: 219 g/mol.

8.5.4.21 (2-Methoxy-2-phenylethyl)(phenyl)selane (210)[142]



Synthesised according to GP 6 or 7 with 52 mg (0.1 mmol) diphenyl diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), silver salt (0.21 mmol) and 34 µl styrene (0.30 mmol, 31 mg) with 100 µl dry methanol. After column chromatography (petroleum ether/diethyl ether 50:1) the product was isolated with yields up to 82% (48 mg, 0.174 mmol) as a pale yellow oil. The obtained spectroscopic data are in agreement with literature data.

R_f (E/PE 1:3) = 0.55.

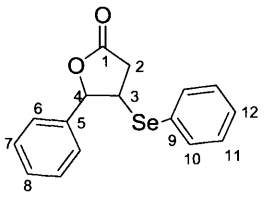
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41–7.39 (m, 2H, Ar*H*), 7.27–7.28 (m, 1H, Ar*H*), 7.25–7.26 (m, 1H, Ar*H*), 7.22–7.25 (m, 2H, Ar*H*), 7.20–7.21 (m, 1H, Ar*H*), 7.17–7.14 (m, 3H, Ar*H*), 4.27 (dd, J = 5.0 Hz, J = 8.0 Hz, 1H, C*H*OCH_3), 3.24 (dd, J = 5.0 Hz, J = 12.0 Hz, 1H, SeCH*H*CH), 3.16 (s, 3H, CHOCH_3), 3.02 (dd, J = 5.0 Hz, J = 12.0 Hz, 1H, SeC*H*HCH) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ = 139.9 (*C*), 131.6 (*C*), 128.0 (*C*H), 127.5 (*C*H), 127.1 (*C*H), 125.8 (*C*H), 125.7 (*C*H), 120.8 (*C*H), 82.2 (*C*HOCH_3), 56.0 (CHOCH_3), 34.4 (Se*C*H).

HPLC: Column: *Chiracel® OD-H*; Solvents: hexane/i-propanol 97:3; Flow rate: 0.5 ml/min; Temperature: 10 °C; Detector: 217 nm; t_R: 9.72 min, t_R: 10.43 min.

$C_{15}H_{16}OSe$: 291 g/mol.

8.5.4.22 *rac*-Dihydro-5-phenyl-4-(phenylselanyl)furan-2(3H)-one (212)[143]



Synthesised according to GP 7 with 52 mg (0.1 mmol) diphenyl diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), (*S*)-(+)-1,1'-binaphtyl-2,2-diyl silver phosphate (0.21 mmol) and 63 mg (*E*)-4-phenylbut-3-enoic acid (0.2 mmol) in dichloromethane. After column chromatography (petroleum ether/diethyl ether 30:1) the racemic product was isolated with 26% yield (17 mg, 0.052 mmol) as a pale yellow oil. The obtained spectroscopic data are in agreement with literature data.

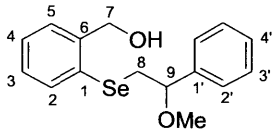
R_f (E/PE 1:3) = 0.46.

^{1}H NMR (500 MHz, $CDCl_3$): 7.46–7.47 (m, 2H, Ar*H*), 7.27–7.32 (m, 4H, Ar*H*), 7.21–7.26 (m, 4H, Ar*H*), 5.31 (d, *J* = 7.0 Hz, 1H, C*H*-4), 3.67 (dd, *J* = 8.0 Hz, *J* = 15.0 Hz, 1H, C*H*-3), 2.97(dd, *J* = 8.0 Hz, *J* = 18.0 Hz, 1H, CH_2-2), 2.60 (dd, *J* = 8.0 Hz, *J* = 18.0 Hz, 1H, CH_2-2) ppm.

HPLC: Column: *Chiracel® OB-H*; Solvents: hexane/i-propanol 60:40; Flow rate: 0.5 ml/min; Detector: 211 nm; t_R: 42.20 min, t_R: 48.90 min.

$C_{16}H_{14}O_2Se$: 317 g/mol.

8.5.4.23 (2-Methoxy-2-phenylethyl)(2-hydroxymethylphenyl)selane (214)



Synthesised according to GP 7 with 52 mg (0.1 mmol) Bis-(2-hydroxybenzyl) diselenide, 0.1 mmol Br_2 (0.1 ml, 1 M solution in CCl_4), chiral acid (0.21 mmol) and 34 µl styrene (0.30 mmol, 31 mg) with dry methanol. After column chromatography (petroleum ether/diethyl ether 20:1) the racemic product was isolated with yields up to 26% as pale yellow oil. The obtained spectroscopic data are in agreement with literature data.

R_f (E/Hex 10:1) = 0.11.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (dd, *J* = 1.3 Hz, *J* = 7.6 Hz, 1H, Ar*H*), 7.26–7.20 (m, 7H, Ar*H*), 7.20 (dt, *J* = 1.6 Hz, *J* = 7.5 Hz, 1H, Ar*H*), 4.77 (dq, *J* = 5.8 Hz, *J* = 12.8 Hz, 2H, CH_2OH), 4.32 (dd, *J* = 4.4 Hz, *J* = 8.8 Hz, 1H, C*H*OCH_3), 3.26 (dd, *J* = 8.8 Hz, *J* = 12.4 Hz, 1H, SeCH_2CH), 3.21 (s, 3H, OCH_3), 3.13 (dd, *J* = 4.4 Hz, *J* = 12.4 Hz, 1H, SeCH_2CH) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.2 (*C*), 141.0 (*C*), 135.0 (*C*H), 130.7 (*C*), 129.2 (*C*H), 129.0 (*C*H), 129.0 (*C*H), 128.6 (*C*H), 128.3 (*C*H), 127.0 (*C*H), 83.2 (*C*HOCH$_3$), 66.1 (*C*H$_2$OH), 57.3 (OC*H*$_3$), 36.4 (Se*C*H) ppm.

IR (KBr): $\tilde{\nu}$ = 3408, 3059, 2931, 2823, 1587, 1492, 1454, 1193, 1104, 1028, 955, 751, 701 cm^{-1}.

MS (EI+) m/z (%): 340 ([M+NH$_4$]$^+$, 46), 291 (100), 273 (21), 258 (10), 195 (5).

HRMS (ES+): [M+NH$_4$]$^+$ calculated for $C_{16}H_{22}O_2N^{76}Se$: 336.0837; found 336.0842.

HPLC: Column: *Chiracel® OD-H*; Solvents: hexane/i-propanol 97:3; Flow rate: 0.5 ml/min; Temperature: 10 °C; Detector: 216 nm; t_R: 26.88 min, t_R: 29.97 min.

$C_{16}H_{18}O_2Se$: 321 g/mol.

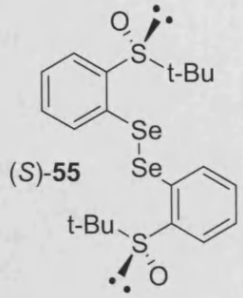
8.5.5 GPx mimics

HPLC Assay: The GPx-like activity was measured using High Pressure Liquid Chromatography (HPLC) consisting of a 2695 separation module, a 2996 photodiode array detector and fraction collector. The assays were performed in 1.8 ml sample vials and a built-in autosampler was used for sample injection. A mixture containing a 1:2 molar ratio of PhSH and peroxide in methanol at room temperature was employed as model system. Runs with and without catalyst were carried out under the same conditions. Periodically, aliquots were injected into the reverse phase column and eluted with methanol and water (9:1), and the concentrations of the product diphenyl disulfide (PhSSPh) were determined at 254 nm using pure PhSSPh as an external standard. The amount of disulfide formed during the course of reaction was calculated from the calibration plot for the standard (PhSSPh).

GSH-GSSG Coupled Assay: The GPx activity was followed spectrophotometrically by following the literature procedure with minor modifications.[131] The test mixture contained GSH (2.0 mM), EDTA (1.0 mM), glutathione reductase (1.0 unit/ml) and NADPH (0.4 mM) in 0.1 M potassium phosphate buffer of pH 7.5. Test compounds (80.0 μM) were added to the assay mixture at room temperature and the reaction was started by the addition of peroxide (1.6 mM). The initial reduction rates were calculated from the rate of NADPH oxidation at 340 nm in the GSH assay. Each initial rate was measured at least 3 times and calculated from the first 5-10% of the reaction by using $\xi_{mM} = 6.22\ mM^{-1}cm^{-1}$ as the millimolar extinction coefficient for NADPH at 340 nm. For the peroxidase activity, the rates were corrected for the background reaction between peroxide and thiol.

Appendix

Single Crystal X-Ray Structure of Compound (*S*)-55



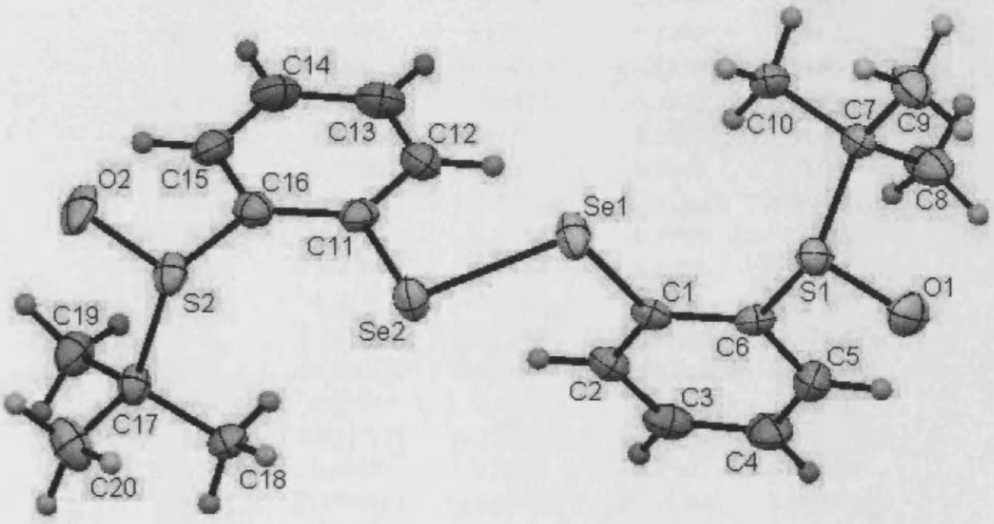


Table 1. Crystal data and structure refinement for Compound (*S*)-**55**.

Identification code	tw808		
Melting Point	118.5–119.5 °C	Absorption coefficient	3.618 mm^{-1}
Empirical formula	$C_{20}H_{26}O_2S_2Se_2$	F(000)	524
Formula Weight	520.45	Crystal size	0.40 x 0.40 x 0.15 mm^3
Temperature	150(2)	Theta range for data collection	2.50° to 27.46°
Wavelength	0.71073	Index ranges	-10<=h<=10
Creation method	SHELXL-97		-13<=k<=13
Crystal System	monoclinic		-16<=l<=13
Space group	P21	Refections collected	4781
Unit cell dimensions	a = 8.3550(3) Å	Independent refections	4314 [R(int) = 0.0389]
	b = 10.4060(3) Å	Completeness to theta = 27.46°	99.9%
	c = 12.8010(5) Å	Refinement method	Full-matrix least-squares on F^2
	α = 90.00	Data / restraints / parameters	4781 / 1 / 241
	β = 103.2810(10)	Godness-of-fit on F2	1.067
	γ = 90.00	Final R indices[I>2sigma(I)]	R1 = 0.0442 wR2 = 0.0762
Volume	1083.18(7) $Å^3$	R indices (all data)	R1 = 0.0361 wR2 = 0.0723
Z	2	Largest diff. peak and hole	0.301 and -0.531 e. $Å^{-3}$
Density (calculated)	1.596 mg/cm^3		

Table 2. Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for compound (*S*)-**55**. U(eq) is defined as one third of the trace of the orthogonalised U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	0.0615(4)	0.0074(4)	0.3391(3)	0.0248(8)
C(2)	-0.0815(5)	-0.0312(4)	0.2688(3)	0.0284(8)
H(2)	-0.1504	0.0309	0.2262	0.034
C(3)	-0.1253(5)	-0.1603(5)	0.2599(4)	0.0336(9)
H(3)	-0.2223	-0.1863	0.2099	0.040
C(4)	-0.0280(5)	-0.2506(5)	0.3236(4)	0.0386(11)
H(4)	-0.0600	-0.3384	0.3189	0.046
C(5)	0.1159(5)	-0.2133(5)	0.3941(4)	0.0369(9)
H(5)	0.1818	-0.2754	0.4386	0.044
C(6)	0.1642(5)	-0.0850(4)	0.3998(3)	0.0249(8)
C(7)	0.5061(5)	-0.0672(4)	0.4100(3)	0.0264(8)
C(8)	0.5037(5)	-0.2061(5)	0.3737(4)	0.0418(10)
H(8A)	0.4039	-0.2220	0.3178	0.063
H(8B)	0.5050	-0.2630	0.4349	0.063
H(8C)	0.6007	-0.2231	0.3449	0.063
C(9)	0.6684(5)	-0.0343(5)	0.4883(4)	0.0405(11)
H(9A)	0.6809	-0.0873	0.5530	0.061
H(9B)	0.6685	0.0567	0.5081	0.061
H(9C)	0.7600	-0.0511	0.4542	0.061
C(10)	0.4726(5)	0.0272(4)	0.3173(4)	0.0382(11)
H(10A)	0.5578	0.0187	0.2765	0.057
H(10B)	0.4735	0.1149	0.3453	0.057
H(10C)	0.3647	0.0089	0.2703	0.057
C(11)	-0.1219(4)	0.3137(4)	0.1461(3)	0.0265(8)
C(12)	-0.0282(5)	0.2390(4)	0.0926(4)	0.0332(9)
H(12)	0.0396	0.1730	0.1305	0.040
C(13)	-0.0317(5)	0.2589(4)	-0.0149(4)	0.0362(11)
H(13)	0.0327	0.2066	-0.0503	0.043
C(14)	-0.1299(6)	0.3558(5)	-0.0708(4)	0.0386(11)
H(14)	-0.1314	0.3709	-0.1442	0.046
C(15)	-0.2256(5)	0.4302(4)	-0.0191(3)	0.0349(10)
H(15)	-0.2925	0.4966	-0.0573	0.042
C(16)	-0.2242(5)	0.4084(4)	0.0882(3)	0.0286(8)
C(17)	-0.5509(5)	0.4402(4)	0.1151(3)	0.0262(8)
C(18)	-0.5412(5)	0.3025(4)	0.1525(3)	0.0300(8)
H(18A)	-0.4905	0.2991	0.2295	0.045
H(18B)	-0.4747	0.2528	0.1131	0.045
H(18C)	-0.6522	0.2660	0.1393	0.045
C(19)	-0.6187(5)	0.4536(4)	-0.0053(3)	0.0358(10)
H(19A)	-0.5644	0.3914	-0.0432	0.054
H(19B)	-0.5981	0.5409	-0.0279	0.054
H(19C)	-0.7374	0.4371	-0.0225	0.054
C(20)	-0.6503(6)	0.5206(5)	0.1773(4)	0.0426(12)
H(20A)	-0.7648	0.4912	0.1603	0.064
H(20B)	-0.6463	0.6112	0.1571	0.064
H(20C)	-0.6038	0.5112	0.2545	0.064

Table 2 (continued). Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for compound (*S*)-**55**. U(eq) is defined as one third of the trace of the orthogonalised U^{ij} tensor.

Atom	x	y	z	U(eq)
O(1)	0.3867(4)	-0.1477(3)	0.5750(2)	0.0425(8)
O(2)	-0.3509(4)	0.6394(3)	0.0972(3)	0.0413(8)
S(1)	0.35240(12)	-0.04263(10)	0.49277(8)	0.0274(2)
S(2)	-0.34121(13)	0.51275(9)	0.15454(8)	0.0278(2)
Se(1)	0.12698(5)	0.18581(4)	0.35951(3)	0.03300(11)
Se(2)	-0.11867(5)	0.29266(4)	0.29724(3)	0.03099(11)

Table 3. Anisotropic displacement parameters ($Å^2$) for compound (*S*)-**55**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11}+...+2hka^*b^*U^{12}]$.

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	0.0216(18)	0.029(2)	0.0257(19)	-0.0022(16)	0.0097(16)	-0.0002(16)
C(2)	0.0204(17)	0.034(2)	0.031(2)	-0.0009(17)	0.0067(16)	-0.0002(17)
C(3)	0.026(2)	0.046(3)	0.030(2)	-0.0062(18)	0.0080(17)	-0.0096(19)
C(4)	0.033(2)	0.032(2)	0.052(3)	-0.0014(19)	0.012(2)	-0.010(2)
C(5)	0.032(2)	0.032(2)	0.047(2)	0.012(2)	0.0095(18)	0.003(2)
C(6)	0.0239(19)	0.026(2)	0.0260(19)	0.0014(16)	0.0092(16)	-0.0056(16)
C(7)	0.0205(18)	0.025(2)	0.035(2)	0.0043(16)	0.0082(16)	0.0010(16)
C(8)	0.033(2)	0.032(2)	0.064(3)	-0.009(2)	0.017(2)	-0.007(2)
C(9)	0.025(2)	0.039(3)	0.056(3)	-0.002(2)	0.006(2)	0.001(2)
C(10)	0.030(2)	0.044(3)	0.044(3)	0.018(2)	0.016(2)	0.0049(19)
C(11)	0.0234(18)	0.029(2)	0.0265(19)	0.0033(16)	0.0043(15)	-0.0061(16)
C(12)	0.025(2)	0.035(2)	0.041(3)	0.0010(19)	0.0104(19)	0.0013(17)
C(13)	0.032(2)	0.043(3)	0.036(2)	-0.0017(19)	0.015(2)	-0.005(2)
C(14)	0.040(3)	0.046(3)	0.034(2)	0.005(2)	0.016(2)	-0.006(2)
C(15)	0.033(2)	0.036(2)	0.035(2)	0.0101(18)	0.0070(19)	-0.0071(19)
C(16)	0.0261(19)	0.028(2)	0.032(2)	-0.0010(17)	0.0073(17)	-0.0042(17)
C(17)	0.0263(19)	0.025(2)	0.025(2)	0.0006(15)	0.0004(16)	0.0004(16)
C(18)	0.0295(19)	0.0236(19)	0.037(2)	0.0041(18)	0.0080(16)	-0.0036(18)
C(19)	0.032(2)	0.037(2)	0.032(2)	0.0057(18)	-0.0062(18)	-0.0056(19)
C(20)	0.035(2)	0.043(3)	0.047(3)	-0.013(2)	0.006(2)	0.009(2)
O(1)	0.0362(16)	0.058(2)	0.0311(16)	0.0200(14)	0.0031(13)	0.0024(15)
O(2)	0.0471(18)	0.0168(13)	0.054(2)	0.0083(13)	-0.0009(15)	-0.0050(13)
S(1)	0.0236(5)	0.0335(6)	0.0241(5)	0.0028(4)	0.0032(4)	0.0000(4)
S(2)	0.0292(5)	0.0193(5)	0.0308(5)	-0.0011(4)	-0.0012(4)	-0.0011(4)
Se(1)	0.02508(19)	0.0258(2)	0.0423(2)	-0.00248(18)	-0.00417(17)	0.00263(19)
Se(2)	0.0295(2)	0.0348(2)	0.0278(2)	0.00223(18)	0.00475(16)	0.00982(19)

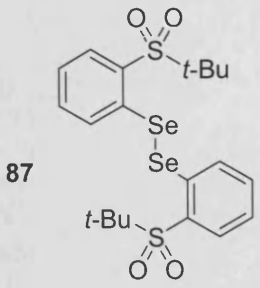
Table 4. Bond lengths [Å] for compound (*S*)-**55**.

Atoms	Distance [Å]	Atoms	Distance [Å]
C(1)-C(2)	1.380(5)	C(11)-Se(2)	1.941(4)
C(1)-C(6)	1.399(6)	C(12)-C(13)	1.385(6)
C(1)-Se(1)	1.936(4)	C(12)-H(12)	0.9500
C(2)-C(3)	1.390(6)	C(13)-C(14)	1.389(6)
C(2)-H(2)	0.9500	C(13)-H(13)	0.9500
C(3)-C(4)	1.379(6)	C(14)-C(15)	1.386(6)
C(3)-H(3)	0.9500	C(14)-H(14)	0.9500
C(4)-C(5)	1.383(6)	C(15)-C(16)	1.389(6)
C(4)-H(4)	0.9500	C(15)-H(15)	0.9500
C(5)-C(6)	1.392(6)	C(16)-S(2)	1.800(4)
C(5)-H(5)	0.9500	C(17)-C(18)	1.507(6)
C(6)-S(1)	1.796(4)	C(17)-C(19)	1.522(5)
C(7)-C(10)	1.516(5)	C(17)-C(20)	1.526(6)
C(7)-C(8)	1.517(6)	C(17)-S(2)	1.868(4)
C(7)-C(9)	1.529(6)	C(18)-H(18A)	0.9800
C(7)-S(1)	1.860(4)	C(18)-H(18B)	0.9800
C(8)-H(8A)	0.9800	C(18)-H(18C)	0.9800
C(8)-H(8B)	0.9800	C(19)-H(19A)	0.9800
C(8)-H(8C)	0.9800	C(19)-H(19B)	0.9800
C(9)-H(9A)	0.9800	C(19)-H(19C)	0.9800
C(9)-H(9B)	0.9800	C(20)-H(20A)	0.9800
C(9)-H(9C)	0.9800	C(20)-H(20B)	0.9800
C(10)-H(10A)	0.9800	C(20)-H(20C)	0.9800
C(10)-H(10B)	0.9800	O(1)-S(1)	1.499(3)
C(10)-H(10C)	0.9800	O(2)-S(2)	1.502(3)
C(11)-C(12)	1.390(5)	Se(1)-Se(2)	2.3092(5)
C(11)-C(16)	1.400(5)		

Table 5. Angles [°] for compound (*S*)-**55**.

Atoms	Angle [°]	Atoms	Angle [°]
C(2)-C(1)-C(6)	119.4(4)	C(13)-C(12)-H(12)	119.3
C(2)-C(1)-Se(1)	122.8(3)	C(11)-C(12)-H(12)	119.3
C(6)-C(1)-Se(1)	117.8(3)	C(12)-C(13)-C(14)	119.7(4)
C(1)-C(2)-C(3)	120.4(4)	C(12)-C(13)-H(13)	120.2
C(1)-C(2)-H(2)	119.8	C(14)-C(13)-H(13)	120.2
C(3)-C(2)-H(2)	119.8	C(15)-C(14)-C(13)	119.8(4)
C(4)-C(3)-C(2)	120.1(4)	C(15)-C(14)-H(14)	120.1
C(4)-C(3)-H(3)	119.9	C(13)-C(14)-H(14)	120.1
C(2)-C(3)-H(3)	119.9	C(14)-C(15)-C(16)	120.4(4)
C(3)-C(4)-C(5)	120.0(4)	C(14)-C(15)-H(15)	119.8
C(3)-C(4)-H(4)	120.0	C(16)-C(15)-H(15)	119.8
C(5)-C(4)-H(4)	120.0	C(15)-C(16)-C(11)	120.3(4)
C(4)-C(5)-C(6)	120.1(4)	C(15)-C(16)-S(2)	119.1(3)
C(4)-C(5)-H(5)	120.0	C(11)-C(16)-S(2)	120.4(3)
C(6)-C(5)-H(5)	120.0	C(18)-C(17)-C(19)	112.9(3)
C(5)-C(6)-C(1)	119.8(4)	C(18)-C(17)-C(20)	110.6(4)
C(5)-C(6)-S(1)	118.0(3)	C(19)-C(17)-C(20)	111.0(4)
C(1)-C(6)-S(1)	122.1(3)	C(18)-C(17)-S(2)	108.7(3)
C(10)-C(7)-C(8)	113.0(4)	C(19)-C(17)-S(2)	110.2(3)
C(10)-C(7)-C(9)	110.2(4)	C(20)-C(17)-S(2)	103.1(3)
C(8)-C(7)-C(9)	111.2(3)	C(17)-C(18)-H(18A)	109.5
C(10)-C(7)-S(1)	109.2(3)	C(17)-C(18)-H(18B)	109.5
C(8)-C(7)-S(1)	110.1(3)	H(18A)-C(18)-H(18B)	109.5
C(9)-C(7)-S(1)	102.7(3)	C(17)-C(18)-H(18C)	109.5
C(7)-C(8)-H(8A)	109.5	H(18A)-C(18)-H(18C)	109.5
C(7)-C(8)-H(8B)	109.5	H(18B)-C(18)-H(18C)	109.5
H(8A)-C(8)-H(8B)	109.5	C(17)-C(19)-H(19A)	109.5
C(7)-C(8)-H(8C)	109.5	C(17)-C(19)-H(19B)	109.5
H(8A)-C(8)-H(8C)	109.5	H(19A)-C(19)-H(19B)	109.5
H(8B)-C(8)-H(8C)	109.5	C(17)-C(19)-H(19C)	109.5
C(7)-C(9)-H(9A)	109.5	H(19A)-C(19)-H(19C)	109.5
C(7)-C(9)-H(9B)	109.5	H(19B)-C(19)-H(19C)	109.5
H(9A)-C(9)-H(9B)	109.5	C(17)-C(20)-H(20A)	109.5
C(7)-C(9)-H(9C)	109.5	C(17)-C(20)-H(20B)	109.5
H(9A)-C(9)-H(9C)	109.5	H(20A)-C(20)-H(20B)	109.5
H(9B)-C(9)-H(9C)	109.5	C(17)-C(20)-H(20C)	109.5
C(7)-C(10)-H(10A)	109.5	H(20A)-C(20)-H(20C)	109.5
C(7)-C(10)-H(10B)	109.5	H(20B)-C(20)-H(20C)	109.5
H(10A)-C(10)-H(10B)	109.5	O(1)-S(1)-C(6)	106.46(19)
C(7)-C(10)-H(10C)	109.5	O(1)-S(1)-C(7)	104.72(18)
H(10A)-C(10)-H(10C)	109.5	C(6)-S(1)-C(7)	101.69(18)
H(10B)-C(10)-H(10C)	109.5	O(2)-S(2)-C(16)	105.8(2)
C(12)-C(11)-C(16)	118.5(4)	O(2)-S(2)-C(17)	106.30(18)
C(12)-C(11)-Se(2)	123.2(3)	C(16)-S(2)-C(17)	101.89(18)
C(16)-C(11)-Se(2)	118.3(3)	C(1)-Se(1)-Se(2)	102.36(11)
C(13)-C(12)-C(11)	121.4(4)	C(11)-Se(2)-Se(1)	101.89(11)

Single Crystal X-Ray Structure of Compound 87



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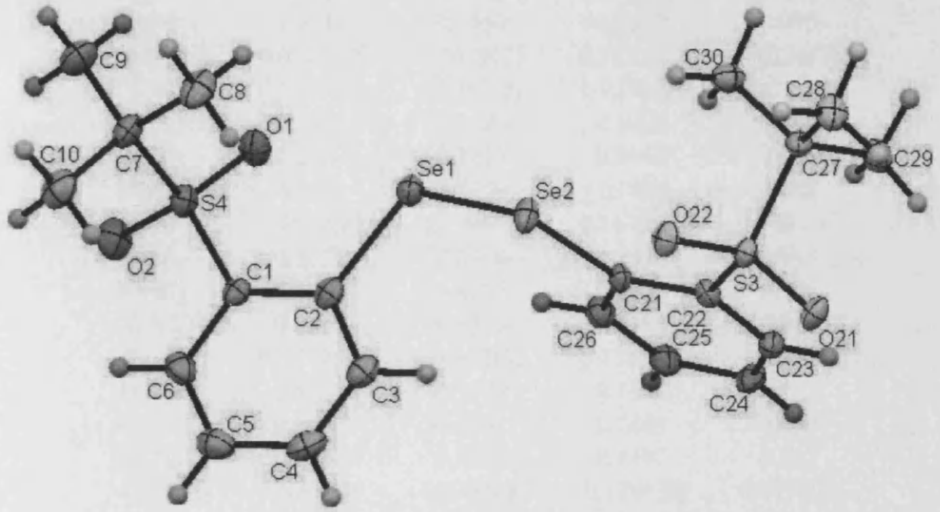


Table 1. Crystal data and structure refinement for Compound **87**.

Identification code	2009src0172		
Melting Point	204–206 °C	Absorption coefficient	3.527 mm^{-1}
Empirical formula	$C_{20}H_{26}O_4S_2Se_2$	F(000)	1112
Formula Weight	552.45	Crystal size	0.33 x 0.23 x 0.09 mm^3
Temperature	120(2)	Theta range for data collection	3.01° to 27.48°
Wavelength	0.71073	Index ranges	-16<=h<=16
Creation method	SHELXL-97		-16<=k<=16
Crystal System	monoclinic		-18<=l<=18
Space group	P21/n	Refections collected	5099
Unit cell dimensions	a = 13.0885(2) Å	Independent refections	3980 [R(int) = 0.0752]
	b = 12.5754(3) Å	Completeness to theta = 27.48°	99.9%
	c = 14.4854(3) Å	Refinement method	Full-matrix least-squares on F^2
	α = 90.00°	Data / restraints / parameters	5099 / 0 / 259
	β = 110.7530(10)°	Godness-of-fit on F2	1.033
	γ = 90.00°	Final R indices[I>2sigma(I)]	R1 = 0.0366 wR2 = 0.0695
Volume	2229.50(8) $Å^3$	R indices (all data)	R1 = 0.0565 wR2 = 0.0758
Z	4	Largest diff. peak and hole	0.445 and 0.109 e. $Å^{-3}$
Density (calculated)	1.646 mg/cm^3		

Table 2. Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for compound **87**. U(eq) is defined as one third of the trace of the orthogonalised U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	0.8001(2)	0.1746(2)	0.1653(2)	0.0173(6)
C(2)	0.7854(2)	0.1027(2)	0.0872(2)	0.0199(7)
C(3)	0.8785(3)	0.0560(3)	0.0787(2)	0.0230(7)
H(3)	0.8708	0.0069	0.0268	0.028
C(4)	0.9820(3)	0.0802(3)	0.1449(3)	0.0268(8)
H(4)	1.0443	0.0481	0.1373	0.032
C(5)	0.9954(3)	0.1505(3)	0.2217(3)	0.0288(8)
H(5)	1.0665	0.1666	0.2668	0.035
C(6)	0.9047(3)	0.1974(3)	0.2326(2)	0.0246(7)
H(6)	0.9134	0.2450	0.2857	0.030
C(7)	0.6715(3)	0.3679(2)	0.1331(2)	0.0221(7)
C(8)	0.6345(3)	0.3557(3)	0.0218(2)	0.0306(8)
H(8A)	0.5682	0.3120	-0.0015	0.046
H(8B)	0.6923	0.3212	0.0043	0.046
H(8C)	0.6189	0.4259	-0.0093	0.046
C(9)	0.5822(3)	0.4196(3)	0.1632(3)	0.0321(8)
H(9A)	0.5659	0.4906	0.1338	0.048
H(9B)	0.6074	0.4255	0.2353	0.048
H(9C)	0.5160	0.3758	0.1398	0.048
C(10)	0.7779(3)	0.4312(3)	0.1747(3)	0.0312(8)
H(10A)	0.8340	0.3979	0.1541	0.047
H(10B)	0.8023	0.4321	0.2469	0.047
H(10C)	0.7654	0.5043	0.1497	0.047
C(21)	0.6904(2)	-0.1485(2)	-0.1201(2)	0.0177(6)
C(22)	0.6975(2)	-0.2181(2)	-0.1936(2)	0.0164(6)
C(23)	0.7110(2)	-0.3273(2)	-0.1761(2)	0.0188(6)
H(23)	0.7183	-0.3729	-0.2257	0.023
C(24)	0.7137(2)	-0.3696(2)	-0.0872(2)	0.0212(7)
H(24)	0.7231	-0.4439	-0.0752	0.025
C(25)	0.7025(3)	-0.3017(3)	-0.0156(2)	0.0234(7)
H(25)	0.7016	-0.3303	0.0447	0.028
C(26)	0.6928(2)	-0.1931(3)	-0.0311(2)	0.0219(7)
H(26)	0.6876	-0.1481	0.0197	0.026
C(27)	0.5487(2)	-0.1842(2)	-0.3935(2)	0.0177(6)
C(28)	0.5490(3)	-0.1505(3)	-0.4949(2)	0.0242(7)
H(28A)	0.5907	-0.2022	-0.5179	0.036
H(28B)	0.5828	-0.0801	-0.4899	0.036
H(28C)	0.4737	-0.1476	-0.5419	0.036
C(29)	0.5087(3)	-0.2980(3)	-0.3957(2)	0.0247(7)
H(29A)	0.4349	-0.3042	-0.4451	0.037
H(29B)	0.5072	-0.3170	-0.3305	0.037
H(29C)	0.5581	-0.3461	-0.4128	0.037
C(30)	0.4822(2)	-0.1067(3)	-0.3557(2)	0.0231(7)
H(30A)	0.4064	-0.1054	-0.4018	0.035
H(30B)	0.5137	-0.0353	-0.3505	0.035
H(30C)	0.4838	-0.1299	-0.2906	0.035

Table 2 (continued). Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for compound **87**. U(eq) is defined as one third of the trace of the orthogonalised U^{ij} tensor.

Atom	x	y	z	U(eq)
O(1)	0.59323(17)	0.17432(18)	0.14210(16)	0.0246(5)
O(2)	0.72566(19)	0.25244(19)	0.29501(16)	0.0297(5)
O(21)	0.75141(17)	-0.25227(17)	-0.34840(16)	0.0217(5)
O(22)	0.72584(17)	-0.06653(17)	-0.30454(16)	0.0218(5)
S(3)	0.69121(6)	-0.17655(6)	-0.31243(5)	0.01659(16)
S(4)	0.69040(6)	0.23662(6)	0.18942(5)	0.01922(17)
Se(1)	0.64071(2)	0.06601(3)	-0.00542(2)	0.02112(9)
Se(2)	0.68259(3)	0.00504(2)	-0.13931(2)	0.02194(9)

Table 3. Anisotropic displacement parameters ($Å^2$) for compound **87**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11}+...+2hka^*b^*U^{12}]$.

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	0.0210(15)	0.0144(15)	0.0176(15)	0.0028(12)	0.0082(12)	0.0020(12)
C(2)	0.0245(16)	0.0144(16)	0.0232(17)	0.0027(13)	0.0112(13)	-0.0009(12)
C(3)	0.0271(17)	0.0191(17)	0.0258(17)	0.0021(14)	0.0130(14)	0.0024(13)
C(4)	0.0257(17)	0.0240(18)	0.034(2)	0.0079(15)	0.0141(15)	0.0077(14)
C(5)	0.0218(17)	0.0262(19)	0.034(2)	0.0060(16)	0.0041(14)	-0.0021(14)
C(6)	0.0270(17)	0.0233(18)	0.0194(17)	0.0016(14)	0.0032(13)	-0.0015(14)
C(7)	0.0275(17)	0.0159(16)	0.0264(17)	0.0004(13)	0.0141(14)	0.0031(13)
C(8)	0.046(2)	0.0227(18)	0.0258(18)	0.0069(15)	0.0165(16)	0.0072(16)
C(9)	0.0321(19)	0.032(2)	0.037(2)	-0.0010(17)	0.0176(16)	0.0073(16)
C(10)	0.0333(19)	0.0193(18)	0.045(2)	0.0010(16)	0.0182(17)	-0.0036(15)
C(21)	0.0172(15)	0.0130(15)	0.0219(16)	-0.0048(12)	0.0057(12)	-0.0031(12)
C(22)	0.0167(14)	0.0173(16)	0.0142(15)	-0.0011(12)	0.0041(12)	-0.0025(12)
C(23)	0.0205(15)	0.0163(16)	0.0179(16)	-0.0013(13)	0.0046(12)	0.0007(12)
C(24)	0.0253(16)	0.0140(16)	0.0238(17)	0.0034(13)	0.0081(13)	0.0034(13)
C(25)	0.0282(17)	0.0222(17)	0.0167(16)	0.0031(14)	0.0043(13)	0.0007(14)
C(26)	0.0247(16)	0.0221(17)	0.0178(16)	-0.0004(13)	0.0062(13)	-0.0010(13)
C(27)	0.0192(15)	0.0165(16)	0.0162(15)	0.0002(12)	0.0047(12)	0.0010(12)
C(28)	0.0323(18)	0.0237(18)	0.0184(16)	0.0023(14)	0.0111(14)	-0.0015(14)
C(29)	0.0246(17)	0.0220(17)	0.0254(18)	-0.0013(14)	0.0062(14)	-0.0043(14)
C(30)	0.0205(16)	0.0284(19)	0.0208(17)	0.0014(14)	0.0077(13)	0.0036(14)
O(1)	0.0248(12)	0.0250(12)	0.0275(13)	-0.0037(10)	0.0137(10)	-0.0058(10)
O(2)	0.0410(14)	0.0339(14)	0.0175(12)	0.0005(10)	0.0143(10)	-0.0002(11)
O(21)	0.0250(11)	0.0185(12)	0.0258(12)	-0.0020(9)	0.0142(9)	0.0025(9)
O(22)	0.0264(12)	0.0159(11)	0.0256(12)	-0.0013(9)	0.0121(9)	-0.0040(9)
S(3)	0.0196(4)	0.0138(4)	0.0181(4)	-0.0003(3)	0.0088(3)	-0.0010(3)
S(4)	0.0241(4)	0.0193(4)	0.0168(4)	-0.0004(3)	0.0104(3)	-0.0009(3)
Se(1)	0.02196(16)	0.01922(17)	0.02218(17)	-0.00493(13)	0.00784(13)	-0.00088(13)
Se(2)	0.03297(19)	0.01372(16)	0.02007(17)	-0.00208(13)	0.01058(14)	-0.00086(13)

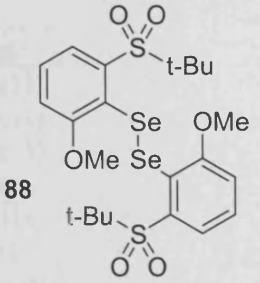
Table 4. Bond lengths [Å] for compound **87**.

Atoms	Distance [Å]	Atoms	Distance [Å]
C(1)-C(6)	1.400(4)	C(22)-C(23)	1.396(4)
C(1)-C(2)	1.407(4)	C(22)-S(3)	1.773(3)
C(1)-S(4)	1.775(3)	C(23)-C(24)	1.382(4)
C(2)-C(3)	1.397(4)	C(23)-H(23)	0.9500
C(2)-Se(1)	1.949(3)	C(24)-C(25)	1.390(4)
C(3)-C(4)	1.388(4)	C(24)-H(24)	0.9500
C(3)-H(3)	0.9500	C(25)-C(26)	1.382(4)
C(4)-C(5)	1.384(5)	C(25)-H(25)	0.9500
C(4)-H(4)	0.9500	C(26)-H(26)	0.9500
C(5)-C(6)	1.383(5)	C(27)-C(29)	1.521(4)
C(5)-H(5)	0.9500	C(27)-C(28)	1.531(4)
C(6)-H(6)	0.9500	C(27)-C(30)	1.531(4)
C(7)-C(8)	1.518(4)	C(27)-S(3)	1.820(3)
C(7)-C(10)	1.530(4)	C(28)-H(28A)	0.9800
C(7)-C(9)	1.531(4)	C(28)-H(28B)	0.9800
C(7)-S(4)	1.820(3)	C(28)-H(28C)	0.9800
C(8)-H(8A)	0.9800	C(29)-H(29A)	0.9800
C(8)-H(8B)	0.9800	C(29)-H(29B)	0.9800
C(8)-H(8C)	0.9800	C(29)-H(29C)	0.9800
C(9)-H(9A)	0.9800	C(30)-H(30A)	0.9800
C(9)-H(9B)	0.9800	C(30)-H(30B)	0.9800
C(9)-H(9C)	0.9800	C(30)-H(30C)	0.9800
C(10)-H(10A)	0.9800	O(1)-S(4)	1.443(2)
C(10)-H(10B)	0.9800	O(2)-S(4)	1.446(2)
C(10)-H(10C)	0.9800	O(21)-S(3)	1.446(2)
C(21)-C(26)	1.396(4)	O(22)-S(3)	1.448(2)
C(21)-C(22)	1.408(4)	Se(1)-Se(2)	2.3245(4)
C(21)-Se(2)	1.948(3)		

Table 5. Angles [°] for compound **87**.

Atoms	Angle [°]	Atoms	Angle [°]
C(6)-C(1)-C(2)	120.9(3)	C(24)-C(23)-H(23)	119.7
C(6)-C(1)-S(4)	115.7(2)	C(22)-C(23)-H(23)	119.7
C(2)-C(1)-S(4)	123.4(2)	C(23)-C(24)-C(25)	118.9(3)
C(3)-C(2)-C(1)	117.7(3)	C(23)-C(24)-H(24)	120.5
C(3)-C(2)-Se(1)	120.3(2)	C(25)-C(24)-H(24)	120.5
C(1)-C(2)-Se(1)	121.9(2)	C(26)-C(25)-C(24)	120.9(3)
C(4)-C(3)-C(2)	121.1(3)	C(26)-C(25)-H(25)	119.5
C(4)-C(3)-H(3)	119.5	C(24)-C(25)-H(25)	119.5
C(2)-C(3)-H(3)	119.5	C(25)-C(26)-C(21)	121.2(3)
C(5)-C(4)-C(3)	120.6(3)	C(25)-C(26)-H(26)	119.4
C(5)-C(4)-H(4)	119.7	C(21)-C(26)-H(26)	119.4
C(3)-C(4)-H(4)	119.7	C(29)-C(27)-C(28)	111.0(3)
C(6)-C(5)-C(4)	119.7(3)	C(29)-C(27)-C(30)	111.8(3)
C(6)-C(5)-H(5)	120.2	C(28)-C(27)-C(30)	111.3(3)
C(4)-C(5)-H(5)	120.2	C(29)-C(27)-S(3)	109.2(2)
C(5)-C(6)-C(1)	120.1(3)	C(28)-C(27)-S(3)	104.7(2)
C(5)-C(6)-H(6)	120.0	C(30)-C(27)-S(3)	108.6(2)
C(1)-C(6)-H(6)	120.0	C(27)-C(28)-H(28A)	109.5
C(8)-C(7)-C(10)	112.0(3)	C(27)-C(28)-H(28B)	109.5
C(8)-C(7)-C(9)	110.9(3)	H(28A)-C(28)-H(28B)	109.5
C(10)-C(7)-C(9)	110.3(3)	C(27)-C(28)-H(28C)	109.5
C(8)-C(7)-S(4)	109.0(2)	H(28A)-C(28)-H(28C)	109.5
C(10)-C(7)-S(4)	109.6(2)	H(28B)-C(28)-H(28C)	109.5
C(9)-C(7)-S(4)	104.7(2)	C(27)-C(29)-H(29A)	109.5
C(7)-C(8)-H(8A)	109.5	C(27)-C(29)-H(29B)	109.5
C(7)-C(8)-H(8B)	109.5	H(29A)-C(29)-H(29B)	109.5
H(8A)-C(8)-H(8B)	109.5	C(27)-C(29)-H(29C)	109.5
C(7)-C(8)-H(8C)	109.5	H(29A)-C(29)-H(29C)	109.5
H(8A)-C(8)-H(8C)	109.5	H(29B)-C(29)-H(29C)	109.5
H(8B)-C(8)-H(8C)	109.5	C(27)-C(30)-H(30A)	109.5
C(7)-C(9)-H(9A)	109.5	C(27)-C(30)-H(30B)	109.5
C(7)-C(9)-H(9B)	109.5	H(30A)-C(30)-H(30B)	109.5
H(9A)-C(9)-H(9B)	109.5	C(27)-C(30)-H(30C)	109.5
C(7)-C(9)-H(9C)	109.5	H(30A)-C(30)-H(30C)	109.5
H(9A)-C(9)-H(9C)	109.5	H(30B)-C(30)-H(30C)	109.5
H(9B)-C(9)-H(9C)	109.5	O(21)-S(3)-O(22)	117.55(13)
C(7)-C(10)-H(10A)	109.5	O(21)-S(3)-C(22)	108.17(13)
C(7)-C(10)-H(10B)	109.5	O(22)-S(3)-C(22)	107.43(13)
H(10A)-C(10)-H(10B)	109.5	O(21)-S(3)-C(27)	107.32(13)
C(7)-C(10)-H(10C)	109.5	O(22)-S(3)-C(27)	108.77(13)
H(10A)-C(10)-H(10C)	109.5	C(22)-S(3)-C(27)	107.17(13)
H(10B)-C(10)-H(10C)	109.5	O(1)-S(4)-O(2)	118.30(13)
C(26)-C(21)-C(22)	117.5(3)	O(1)-S(4)-C(1)	107.85(14)
C(26)-C(21)-Se(2)	120.9(2)	O(2)-S(4)-C(1)	106.96(14)
C(22)-C(21)-Se(2)	121.5(2)	O(1)-S(4)-C(7)	108.83(14)
C(23)-C(22)-C(21)	120.8(3)	O(2)-S(4)-C(7)	106.94(15)
C(23)-C(22)-S(3)	115.2(2)	C(1)-S(4)-C(7)	107.51(14)
C(21)-C(22)-S(3)	124.0(2)	C(2)-Se(1)-Se(2)	101.18(9)
C(24)-C(23)-C(22)	120.5(3)	C(21)-Se(2)-Se(1)	102.90(9)

Single Crystal X-Ray Structure of Compound 88



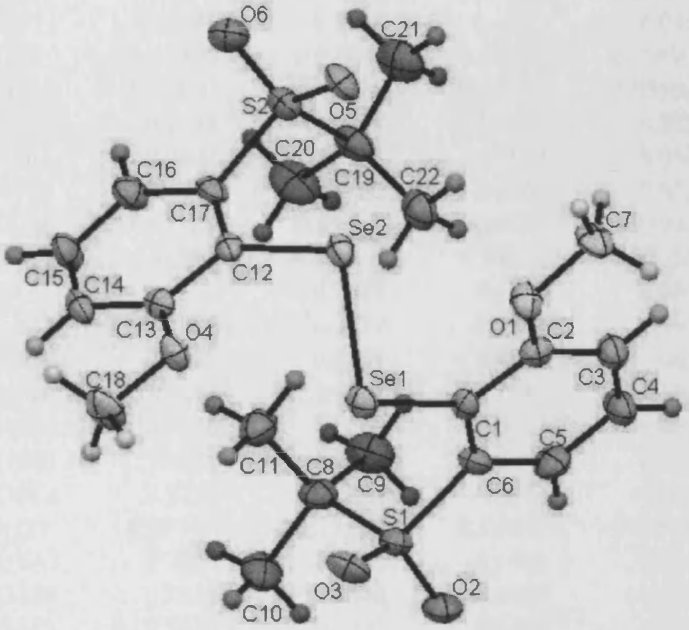


Table 1. Crystal data and structure refinement for Compound **88**.

Identification code	tw0919		
Melting Point	253–256 °C	Absorption coefficient	3.019 mm^{-1}
Empirical formula	$C_{22}H_{30}O_6S_2Se_2$	F(000)	620
Formula Weight	672.18	Crystal size	0.30 x 0.05 x 0.03 mm^3
Temperature	150(2)	Theta range for data collection	2.54° to 27.54°
Wavelength	0.71073	Index ranges	-11<=h<=10
Creation method	SHELXL-97		-20<=k<=23
Crystal System	Triclinic		-23<=l<=23
Space group	P-1	Refections collected	12561
Unit cell dimensions	a = 8.5696(2) Å	Independent refections	8261 [R(int) = 0.0525]
	b = 17.8047(3) Å	Completeness to theta = 27.54°	99.0%
	c = 18.2644(4) Å	Refinement method	Full-matrix least-squares on F^2
	α = 90.3780(10)	Data / restraints / parameters	12561 / 91 / 666
	β = 95.4640(10)	Godness-of-fit on F^2	1.027
	γ = 97.0250(10)	Final R indices[I >2sigma(1)]	R1 = 0.1116 wR2 = 0.1282
Volume	2752.81(10) $Å^3$	R indices (all data)	R1 = 0.0610 wR2 = 0.1096
Z	4	Largest diff. peak and hole	0.725 and -1.103 e. $Å^{-3}$
Density (calculated)	1.622 Mg/cm3		

Table 2. Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for compound **88**. U(eq) is defined as one third of the trace of the orthogonalised U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	0.5831(6)	0.4114(3)	0.5984(3)	0.0211(11)
C(2)	0.4348(6)	0.4359(3)	0.5990(3)	0.0250(11)
C(3)	0.3235(7)	0.4248(3)	0.5379(3)	0.0312(13)
H(3)	0.2216	0.4402	0.5398	0.037
C(4)	0.3611(7)	0.3914(3)	0.4744(3)	0.0362(14)
H(4)	0.2852	0.3842	0.4328	0.043
C(5)	0.5088(7)	0.3683(3)	0.4714(3)	0.0333(13)
H(5)	0.5349	0.3456	0.4277	0.040
C(6)	0.6189(6)	0.3786(3)	0.5328(3)	0.0245(11)
C(7)	0.2512(7)	0.4919(3)	0.6675(3)	0.0349(14)
H(7A)	0.2252	0.5265	0.6279	0.052
H(7B)	0.2477	0.5169	0.7152	0.052
H(7C)	0.1745	0.4462	0.6631	0.052
C(8)	0.8193(7)	0.2558(3)	0.5469(3)	0.0304(13)
C(9)	0.6790(7)	0.2061(3)	0.5084(3)	0.0432(15)
H(9A)	0.6893	0.1529	0.5188	0.065
H(9B)	0.6756	0.2138	0.4553	0.065
H(9C)	0.5815	0.2193	0.5263	0.065
C(10)	0.9765(7)	0.2360(4)	0.5215(3)	0.0422(15)
H(10A)	0.9920	0.1844	0.5363	0.063
H(10B)	10.641	0.2716	0.5442	0.063
H(10C)	0.9730	0.2393	0.4678	0.063
C(11)	0.8238(8)	0.2510(3)	0.6307(3)	0.0386(15)
H(11A)	0.7254	0.2655	0.6466	0.058
H(11B)	0.9134	0.2855	0.6535	0.058
H(11C)	0.8354	0.1991	0.6457	0.058
C(12)	0.6801(6)	0.2969(3)	0.8020(2)	0.0208(11)
C(13)	0.8449(6)	0.3091(3)	0.8196(3)	0.0231(11)
C(14)	0.9312(6)	0.2489(3)	0.8370(3)	0.0267(12)
H(14)	10.428	0.2578	0.8473	0.032
C(15)	0.8533(7)	0.1760(3)	0.8390(3)	0.0332(13)
H(15)	0.9122	0.1347	0.8487	0.040
C(16)	0.6932(7)	0.1633(3)	0.8271(3)	0.0317(13)
H(16)	0.6406	0.1136	0.8316	0.038
C(17)	0.6047(6)	0.2231(3)	0.8084(3)	0.0243(11)
C(18)	1.0792(7)	0.3984(3)	0.8396(4)	0.0416(15)
H(18A)	11.051	0.3804	0.8893	0.062
H(18B)	11.108	0.4531	0.8382	0.062
H(18C)	11.357	0.3726	0.8047	0.062
C(19)	0.3303(7)	0.1656(3)	0.7062(3)	0.0325(13)
C(20)	0.4293(8)	0.1047(4)	0.6844(4)	0.0462(17)
H(20A)	0.3911	0.0856	0.6347	0.069
H(20B)	0.4201	0.0630	0.7191	0.069
H(20C)	0.5402	0.1265	0.6854	0.069
C(21)	0.1571(7)	0.1320(4)	0.7091(4)	0.0470(16)
H(21A)	0.0963	0.1715	0.7245	0.071
H(21B)	0.1514	0.0908	0.7444	0.071
H(21C)	0.1132	0.1124	0.6602	0.071
C(22)	0.3449(7)	0.2328(3)	0.6556(3)	0.0388(14)
H(22A)	0.3065	0.2162	0.6051	0.058
H(22B)	0.4559	0.2546	0.6573	0.058

Table 2 (continued). Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for compound **88**. U(eq) is defined as one third of the trace of the orthogonalised U^{ij} tensor.

Atom	x	y	z	U(eq)
H(22C)	0.2818	0.2711	0.6717	0.058
O(1)	0.4076(4)	0.4716(2)	0.66202(19)	0.0296(9)
O(2)	0.8200(5)	0.3530(2)	0.4403(2)	0.0393(10)
O(3)	0.9272(4)	0.4028(2)	0.5642(2)	0.0367(9)
O(4)	0.9125(4)	0.38233(19)	0.81993(19)	0.0276(8)
O(5)	0.3222(4)	0.26423(19)	0.8160(2)	0.0296(9)
O(6)	0.3663(5)	0.1336(2)	0.8478(2)	0.0359(9)
S(1)	0.81039(16)	0.35367(8)	0.51886(7)	0.0284(3)
S(2)	0.39554(16)	0.19770(7)	0.80105(7)	0.0261(3)
Se(1)	0.73268(6)	0.43042(3)	0.68457(3)	0.02600(13)
Se(2)	0.56835(6)	0.38164(3)	0.77325(3)	0.02447(13)

Table 3. Anisotropic displacement parameters ($Å^2$) for compound **88**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11}+...+2hka^*b^*U^{12}]$.

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	0.018(3)	0.020(2)	0.022(3)	0.000(2)	-0.004(2)	-0.003(2)
C(2)	0.027(3)	0.023(3)	0.025(3)	0.000(2)	0.004(2)	0.002(2)
C(3)	0.025(3)	0.041(3)	0.028(3)	0.000(2)	-0.001(2)	0.007(3)
C(4)	0.024(3)	0.058(4)	0.026(3)	-0.002(3)	-0.002(2)	0.007(3)
C(5)	0.037(4)	0.044(3)	0.019(3)	-0.001(2)	0.005(2)	0.004(3)
C(6)	0.019(3)	0.030(3)	0.026(3)	-0.001(2)	0.007(2)	0.001(2)
C(7)	0.029(3)	0.048(3)	0.030(3)	-0.009(3)	0.008(3)	0.013(3)
C(8)	0.031(3)	0.036(3)	0.026(3)	-0.002(2)	0.009(2)	0.005(3)
C(9)	0.041(4)	0.044(4)	0.044(4)	-0.010(3)	0.008(3)	-0.001(3)
C(10)	0.041(4)	0.055(4)	0.035(3)	-0.003(3)	0.011(3)	0.020(3)
C(11)	0.045(4)	0.042(3)	0.032(3)	0.006(3)	0.010(3)	0.014(3)
C(12)	0.020(3)	0.028(3)	0.015(2)	-0.003(2)	0.001(2)	0.007(2)
C(13)	0.021(3)	0.030(3)	0.017(2)	-0.004(2)	-0.001(2)	0.000(2)
C(14)	0.017(3)	0.039(3)	0.025(3)	-0.006(2)	-0.002(2)	0.009(2)
C(15)	0.023(3)	0.030(3)	0.048(4)	0.003(3)	0.002(3)	0.012(2)
C(16)	0.027(3)	0.033(3)	0.037(3)	-0.001(2)	0.007(3)	0.009(3)
C(17)	0.016(3)	0.037(3)	0.022(3)	-0.002(2)	0.006(2)	0.006(2)
C(18)	0.021(3)	0.034(3)	0.066(4)	0.003(3)	-0.002(3)	-0.007(3)
C(19)	0.022(3)	0.044(3)	0.031(3)	-0.013(3)	0.001(2)	-0.001(3)
C(20)	0.044(4)	0.051(4)	0.045(4)	-0.024(3)	0.010(3)	0.011(3)
C(21)	0.036(4)	0.055(4)	0.046(4)	-0.013(3)	-0.001(3)	-0.009(3)
C(22)	0.030(4)	0.052(4)	0.033(3)	-0.005(3)	-0.004(3)	0.005(3)
O(1)	0.031(2)	0.033(2)	0.0269(19)	-0.0053(16)	0.0006(17)	0.0132(17)
O(2)	0.033(2)	0.060(3)	0.028(2)	0.0045(19)	0.0138(18)	0.010(2)
O(3)	0.021(2)	0.041(2)	0.046(2)	-0.0031(19)	0.0082(18)	-0.0045(18)
O(4)	0.019(2)	0.029(2)	0.033(2)	-0.0040(16)	-0.0047(16)	0.0015(16)
O(5)	0.020(2)	0.031(2)	0.038(2)	-0.0076(16)	0.0023(17)	0.0075(16)
O(6)	0.031(2)	0.039(2)	0.039(2)	0.0053(18)	0.0083(18)	0.0011(18)
S(1)	0.0218(7)	0.0385(8)	0.0259(7)	0.0023(6)	0.0070(6)	0.0034(6)
S(2)	0.0198(7)	0.0314(7)	0.0271(7)	-0.0055(5)	0.0022(6)	0.0032(6)
Se(1)	0.0209(3)	0.0307(3)	0.0245(3)	-0.0035(2)	-0.0018(2)	-0.0007(2)
Se(2)	0.0211(3)	0.0298(3)	0.0235(3)	-0.0025(2)	0.0006(2)	0.0088(2)

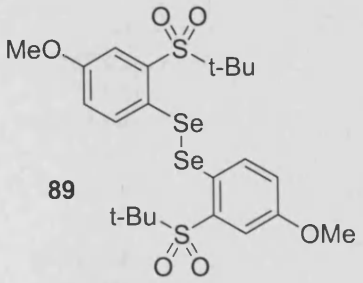
Table 4. Bond lengths [Å] for compound **88**.

Atoms	Distance [Å]	Atoms	Distance [Å]
C(1)-C(2)	1.394(7)	C(13)-O(4)	1.360(6)
C(1)-C(6)	1.406(7)	C(13)-C(14)	1.397(7)
C(1)-Se(1)	1.933(5)	C(14)-C(15)	1.388(8)
C(2)-O(1)	1.364(6)	C(15)-C(16)	1.359(8)
C(2)-C(3)	1.394(7)	C(16)-C(17)	1.407(7)
C(3)-C(4)	1.382(7)	C(17)-S(2)	1.786(5)
C(4)-C(5)	1.384(8)	C(18)-O(4)	1.433(6)
C(5)-C(6)	1.391(7)	C(19)-C(22)	1.518(8)
C(6)-S(1)	1.792(5)	C(19)-C(20)	1.528(7)
C(7)-O(1)	1.443(6)	C(19)-C(21)	1.536(8)
C(8)-C(9)	1.514(8)	C(19)-S(2)	1.834(5)
C(8)-C(11)	1.531(7)	O(2)-S(1)	1.445(4)
C(8)-C(10)	1.545(7)	O(3)-S(1)	1.439(4)
C(8)-S(1)	1.828(5)	O(5)-S(2)	1.444(3)
C(12)-C(17)	1.402(7)	O(6)-S(2)	1.441(4)
C(12)-C(13)	1.408(7)	Se(1)-Se(2)	2.3484(8)
C(12)-Se(2)	1.933(5)		

Table 5. Angles [°] for compound **88**.

Atoms	Angle [°]	Atoms	Angle [°]
C(2)-C(1)-C(6)	117.5(4)	C(15)-C(16)-C(17)	120.6(5)
C(2)-C(1)-Se(1)	118.8(4)	C(12)-C(17)-C(16)	120.6(5)
C(6)-C(1)-Se(1)	123.6(4)	C(12)-C(17)-S(2)	124.7(4)
O(1)-C(2)-C(1)	116.0(4)	C(16)-C(17)-S(2)	114.6(4)
O(1)-C(2)-C(3)	123.0(5)	C(22)-C(19)-C(20)	111.6(5)
C(1)-C(2)-C(3)	121.1(5)	C(22)-C(19)-C(21)	111.6(5)
C(4)-C(3)-C(2)	120.1(5)	C(20)-C(19)-C(21)	110.7(5)
C(3)-C(4)-C(5)	120.3(5)	C(22)-C(19)-S(2)	109.2(4)
C(4)-C(5)-C(6)	119.5(5)	C(20)-C(19)-S(2)	109.3(4)
C(5)-C(6)-C(1)	121.5(5)	C(21)-C(19)-S(2)	104.1(4)
C(5)-C(6)-S(1)	114.8(4)	C(2)-O(1)-C(7)	117.8(4)
C(1)-C(6)-S(1)	123.5(4)	C(13)-O(4)-C(18)	118.5(4)
C(9)-C(8)-C(11)	112.0(5)	O(3)-S(1)-O(2)	118.3(3)
C(9)-C(8)-C(10)	111.4(5)	O(3)-S(1)-C(6)	108.6(2)
C(11)-C(8)-C(10)	109.9(5)	O(2)-S(1)-C(6)	106.5(2)
C(9)-C(8)-S(1)	109.0(4)	O(3)-S(1)-C(8)	109.3(2)
C(11)-C(8)-S(1)	109.8(4)	O(2)-S(1)-C(8)	105.3(2)
C(10)-C(8)-S(1)	104.4(4)	C(6)-S(1)-C(8)	108.6(2)
C(17)-C(12)-C(13)	117.4(4)	O(6)-S(2)-O(5)	117.4(2)
C(17)-C(12)-Se(2)	123.2(4)	O(6)-S(2)-C(17)	106.5(2)
C(13)-C(12)-Se(2)	119.3(4)	O(5)-S(2)-C(17)	108.5(2)
O(4)-C(13)-C(14)	122.8(5)	O(6)-S(2)-C(19)	107.3(3)
O(4)-C(13)-C(12)	116.0(4)	O(5)-S(2)-C(19)	108.5(2)
C(14)-C(13)-C(12)	121.1(5)	C(17)-S(2)-C(19)	108.3(2)
C(15)-C(14)-C(13)	119.7(5)	C(1)-Se(1)-Se(2)	98.39(15)
C(16)-C(15)-C(14)	120.4(5)	C(12)-Se(2)-Se(1)	97.54(15)

Single Crystal X-Ray Structure of Compound 89



89

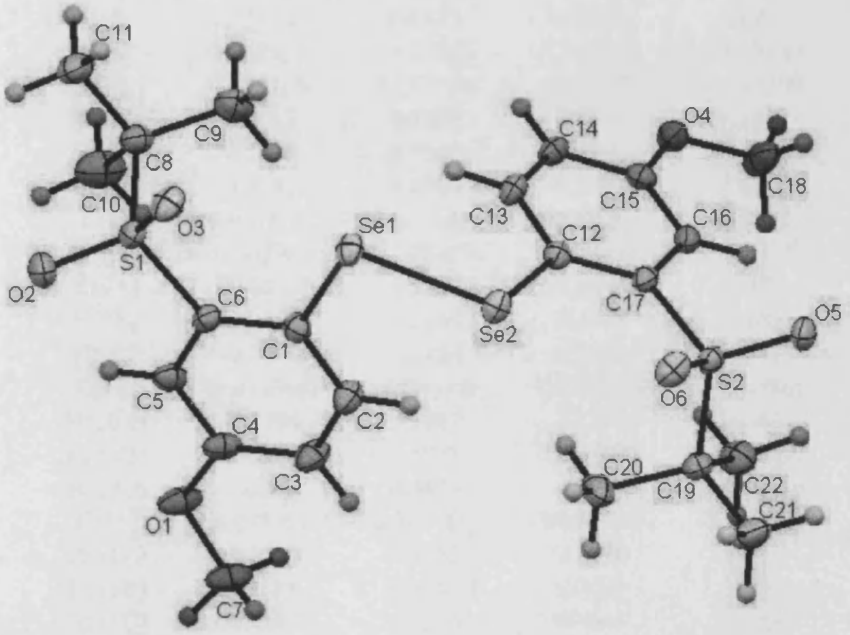


Table 1. Crystal data and structure refinement for Compound **89**.

Identification code	tw0920		
Melting Point	193–196 °C	Absorption coefficient	3.100 mm^{-1}
Empirical formula	$C_{22}H_{30}O_6S_2Se_2$	F(000)	620
Formula Weight	612.50	Crystal size	0.30 x 0.30 x 0.10 mm^3
Temperature	150(2)	Theta range for data collection	2.46° to 27.49°
Wavelength	0.71073	Index ranges	-13<=h<=13
Creation method	SHELXL-97		-13<=k<=13
Crystal System	Triclinic		-15<=l<=17
Space group	P-1	Refections collected	8482
Unit cell dimensions	a = 10.0322(2) Å	Independent refections	5781 [R(int) = 0.0255]
	b = 10.6350(3) Å	Completeness to theta = 27.49°	99.3%
	c = 13.1116(3) Å	Refinement method	Full-matrix least-squares on F^2
	α = 90.3320(10)°	Data / restraints / parameters	5781 / 0 / 298
	β = 107.3160(10)°	Godness-of-fit on F^2	1.033
	γ= 106.5060(10)°	Final R indices[I > 2sigma(I)]	R1 = 0.0418 wR2 = 0.0791
Volume	1274.22(5) $Å^3$	R indices (all data)	R1 = 0.0343 wR2 = 0.0754
Z	2	Largest diff. peak and hole	0.478 and -0.566 e. $Å^{-3}$
Density (calculated)	1.596 mg/cm^3		

Table 2. Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for compound **89**. U(eq) is defined as one third of the trace of the orthogonalised U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	0.2914(3)	0.3900(3)	0.4797(2)	0.0198(5)
C(2)	0.3469(3)	0.4462(3)	0.5853(2)	0.0247(6)
H(2)	0.3604	0.3905	0.6415	0.030
C(3)	0.3834(3)	0.5809(3)	0.6117(2)	0.0276(6)
H(3)	0.4194	0.6159	0.6849	0.033
C(4)	0.3672(3)	0.6642(3)	0.5308(2)	0.0232(6)
C(5)	0.3124(3)	0.6112(3)	0.4244(2)	0.0223(5)
H(5)	0.3012	0.6677	0.3686	0.027
C(6)	0.2739(3)	0.4757(3)	0.3990(2)	0.0190(5)
C(7)	0.4721(3)	0.8571(3)	0.6561(2)	0.0315(7)
H(7A)	0.4012	0.8352	0.6960	0.047
H(7B)	0.5078	0.9530	0.6562	0.047
H(7C)	0.5545	0.8237	0.6902	0.047
C(8)	0.0118(3)	0.3975(3)	0.2139(2)	0.0246(6)
C(9)	-0.0623(3)	0.2991(3)	0.2791(3)	0.0351(7)
H(9A)	-0.0281	0.3359	0.3543	0.053
H(9B)	-0.0379	0.2168	0.2745	0.053
H(9C)	-0.1686	0.2814	0.2504	0.053
C(10)	-0.0149(4)	0.5311(3)	0.2254(3)	0.0419(8)
H(10A)	-0.1194	0.5212	0.1935	0.063
H(10B)	0.0413	0.5948	0.1884	0.063
H(10C)	0.0163	0.5627	0.3017	0.063
C(11)	-0.0387(4)	0.3433(3)	0.0961(2)	0.0361(7)
H(11A)	-0.0202	0.2582	0.0910	0.054
H(11B)	0.0153	0.4053	0.0568	0.054
H(11C)	-0.1437	0.3316	0.0649	0.054
C(12)	0.1361(3)	0.1261(2)	0.6600(2)	0.0184(5)
C(13)	0.0121(3)	0.1440(3)	0.5855(2)	0.0200(5)
H(13)	0.0127	0.1575	0.5141	0.024
C(14)	-0.1112(3)	0.1426(3)	0.6122(2)	0.0201(5)
H(14)	-0.1931	0.1565	0.5599	0.024
C(15)	-0.1157(3)	0.1208(2)	0.7163(2)	0.0192(5)
C(16)	0.0031(3)	0.0983(2)	0.7913(2)	0.0191(5)
H(16)	-0.0006	0.0796	0.8614	0.023
C(17)	0.1285(3)	0.1031(2)	0.7636(2)	0.0178(5)
C(18)	-0.2516(3)	0.0992(4)	0.8392(2)	0.0357(7)
H(18A)	-0.2425	0.0112	0.8539	0.054
H(18B)	-0.3465	0.1033	0.8428	0.054
H(18C)	-0.1728	0.1653	0.8928	0.054
C(19)	0.3768(3)	0.2335(3)	0.9483(2)	0.0221(5)
C(20)	0.4289(4)	0.3357(3)	0.8764(2)	0.0344(7)
H(20A)	0.3440	0.3499	0.8228	0.052
H(20B)	0.4872	0.3040	0.8399	0.052
H(20C)	0.4889	0.4189	0.9201	0.052
C(21)	0.5066(3)	0.2056(3)	1.0327(2)	0.0361(7)
H(21A)	0.5681	0.2869	10.785	0.054
H(21B)	0.5646	0.1732	0.9963	0.054
H(21C)	0.4696	0.1388	10.768	0.054
C(22)	0.2790(3)	0.2757(3)	1.0024(2)	0.0297(6)
H(22A)	0.3365	0.3549	10.521	0.044

Table 2 (continued). Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for compound **89**. U(eq) is defined as one third of the trace of the orthogonalised U^{ij} tensor.

Atom	x	y	z	U(eq)
H(22B)	0.2393	0.2045	10.422	0.044
H(22C)	0.1983	0.2948	0.9477	0.044
O(1)	0.4027(2)	0.79781(19)	0.54749(17)	0.0306(5)
O(2)	0.2749(2)	0.5240(2)	0.20402(16)	0.0328(5)
O(3)	0.2288(2)	0.29279(19)	0.24869(15)	0.0262(4)
O(4)	-0.2416(2)	0.1249(2)	0.73481(15)	0.0245(4)
O(5)	0.2127(2)	-0.01318(19)	0.93556(15)	0.0260(4)
O(6)	0.3703(2)	0.03767(19)	0.81801(15)	0.0247(4)
S(1)	0.20803(7)	0.42057(6)	0.25980(5)	0.02055(15)
S(2)	0.27519(7)	0.07574(6)	0.86791(5)	0.01841(14)
Se(1)	0.24739(3)	0.20064(2)	0.44708(2)	0.02022(9)
Se(2)	0.30666(3)	0.12962(3)	0.61682(2)	0.02025(9)

Table 3. Anisotropic displacement parameters ($Å^2$) for compound **89**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11}+...+2hka^*b^*U^{12}]$.

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	0.0207(12)	0.0209(13)	0.0191(12)	0.0016(10)	0.0083(10)	0.0060(10)
C(2)	0.0329(15)	0.0238(14)	0.0185(13)	0.0020(10)	0.0066(11)	0.0114(12)
C(3)	0.0328(15)	0.0273(15)	0.0199(13)	-0.0033(11)	0.0036(12)	0.0098(12)
C(4)	0.0187(12)	0.0204(13)	0.0275(14)	-0.0041(11)	0.0008(11)	0.0078(10)
C(5)	0.0180(12)	0.0215(13)	0.0245(13)	0.0012(10)	0.0018(10)	0.0065(10)
C(6)	0.0169(12)	0.0227(13)	0.0170(12)	0.0007(10)	0.0042(10)	0.0063(10)
C(7)	0.0269(14)	0.0286(15)	0.0333(16)	-0.0118(12)	-0.0015(12)	0.0115(12)
C(8)	0.0215(13)	0.0229(13)	0.0251(14)	0.0004(11)	0.0021(11)	0.0058(11)
C(9)	0.0245(15)	0.0401(18)	0.0351(17)	0.0036(14)	0.0066(13)	0.0043(13)
C(10)	0.0344(17)	0.0335(17)	0.052(2)	-0.0032(15)	-0.0007(15)	0.0166(14)
C(11)	0.0382(17)	0.0321(16)	0.0249(15)	0.0000(12)	-0.0030(13)	0.0040(14)
C(12)	0.0215(12)	0.0167(12)	0.0172(12)	0.0016(9)	0.0058(10)	0.0064(10)
C(13)	0.0251(13)	0.0215(13)	0.0145(11)	0.0027(10)	0.0043(10)	0.0105(10)
C(14)	0.0210(12)	0.0219(13)	0.0173(12)	0.0027(10)	0.0025(10)	0.0095(10)
C(15)	0.0181(12)	0.0160(12)	0.0222(13)	-0.0007(10)	0.0061(10)	0.0030(10)
C(16)	0.0220(12)	0.0178(12)	0.0165(12)	0.0035(9)	0.0060(10)	0.0045(10)
C(17)	0.0210(12)	0.0145(11)	0.0154(11)	0.0015(9)	0.0026(10)	0.0048(10)
C(18)	0.0233(14)	0.060(2)	0.0205(14)	-0.0015(14)	0.0085(12)	0.0067(14)
C(19)	0.0223(13)	0.0221(13)	0.0178(12)	-0.0013(10)	0.0039(10)	0.0030(10)
C(20)	0.0423(18)	0.0263(15)	0.0262(15)	-0.0015(12)	0.0134(13)	-0.0053(13)
C(21)	0.0277(15)	0.0441(19)	0.0269(15)	-0.0024(13)	-0.0019(13)	0.0073(14)
C(22)	0.0332(16)	0.0282(15)	0.0271(14)	-0.0045(12)	0.0102(12)	0.0078(12)
O(1)	0.0303(11)	0.0207(10)	0.0321(11)	-0.0070(8)	-0.0065(9)	0.0118(8)
O(2)	0.0365(12)	0.0316(11)	0.0237(10)	0.0082(9)	0.0104(9)	-0.0007(9)
O(3)	0.0341(11)	0.0265(10)	0.0204(9)	-0.0009(8)	0.0079(8)	0.0135(9)
O(4)	0.0186(9)	0.0341(11)	0.0216(9)	0.0025(8)	0.0078(8)	0.0077(8)
O(5)	0.0320(11)	0.0239(10)	0.0189(9)	0.0087(8)	0.0051(8)	0.0063(8)
O(6)	0.0267(10)	0.0290(10)	0.0219(9)	0.0004(8)	0.0060(8)	0.0156(8)
S(1)	0.0236(3)	0.0208(3)	0.0157(3)	0.0019(2)	0.0061(2)	0.0043(3)
S(2)	0.0208(3)	0.0183(3)	0.0151(3)	0.0030(2)	0.0028(2)	0.0072(2)
Se(1)	0.02773(15)	0.01938(14)	0.01635(14)	0.00171(10)	0.00919(11)	0.00889(11)
Se(2)	0.02303(14)	0.02353(15)	0.01819(14)	0.00381(10)	0.00739(10)	0.01207(11)

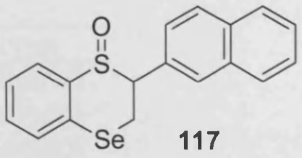
Table 4. Bond lengths [Å] for compound **89**.

Atoms	Distance [Å]	Atoms	Distance [Å]
C(1)-C(2)	1.389(4)	C(13)-C(14)	1.378(4)
C(1)-C(6)	1.404(4)	C(14)-C(15)	1.397(4)
C(1)-Se(1)	1.951(3)	C(15)-O(4)	1.367(3)
C(2)-C(3)	1.388(4)	C(15)-C(16)	1.383(4)
C(3)-C(4)	1.389(4)	C(16)-C(17)	1.398(4)
C(4)-O(1)	1.362(3)	C(17)-S(2)	1.781(3)
C(4)-C(5)	1.386(4)	C(18)-O(4)	1.425(3)
C(5)-C(6)	1.393(4)	C(19)-C(20)	1.525(4)
C(6)-S(1)	1.777(3)	C(19)-C(22)	1.527(4)
C(7)-O(1)	1.435(3)	C(19)-C(21)	1.540(4)
C(8)-C(9)	1.526(4)	C(19)-S(2)	1.826(3)
C(8)-C(11)	1.527(4)	O(2)-S(1)	1.441(2)
C(8)-C(10)	1.533(4)	O(3)-S(1)	1.445(2)
C(8)-S(1)	1.821(3)	O(5)-S(2)	1.441(2)
C(12)-C(13)	1.397(4)	O(6)-S(2)	1.446(2)
C(12)-C(17)	1.401(4)	Se(1)-Se(2)	2.3160(4)
C(12)-Se(2)	1.947(3)		

Table 5. Angles [°] for compound **89**.

Atoms	Angle [°]	Atoms	Angle [°]
C(2)-C(1)-C(6)	117.1(2)	C(15)-C(16)-C(17)	119.7(2)
C(2)-C(1)-Se(1)	120.5(2)	C(16)-C(17)C(12)	121.8(2)
C(6)-C(1)-Se(1)	122.29(19)	C(16)-C(17)-S(2)	115.40(19)
C(3)-C(2)-C(1)	122.3(3)	C(12)-C(17)-S(2)	122.8(2)
C(2)-C(3)-C(4)	119.7(3)	C(20)-C(19)-C(22)	111.3(3)
O(1)-C(4)-C(5)	116.0(2)	C(20)-C(19)-C(21)	111.5(3)
O(1)-C(4)-C(3)	124.6(2)	C(22)-C(19)-C(21)	110.6(2)
C(5)-C(4)-C(3)	119.4(2)	C(20)-C(19)-S(2)	109.35(18)
C(4)-C(5)-C(6)	120.3(3)	C(22)-C(19)-S(2)	109.30(19)
C(5)-C(6)-C(1)	121.1(2)	C(21)-C(19)-S(2)	104.6(2)
C(5)-C(6)-S(1)	115.9(2)	C(4)-O(1)-C(7)	117.5(2)
C(1)-C(6)-S(1)	122.9(2)	C(15)-O(4)-C(18)	116.7(2)
C(9)-C(8)-C(11)	110.9(2)	O(2)-S(1)-O(3)	118.25(13)
C(9)-C(8)-C(10)	111.1(3)	O(2)-S(1)-C(6)	108.06(12)
C(11)-C(8)-C(10)	111.1(3)	O(3)-S(1)-C(6)	107.54(12)
C(9)-C(8)-S(1)	109.6(2)	O(2)-S(1)-C(8)	107.57(13)
C(11)-C(8)-S(1)	104.8(2)	O(3)-S(1)-C(8)	107.43(12)
C(10)-C(8)-S(1)	109.0(2)	C(6)-S(1)-C(8)	107.57(13)
C(13)-C(12)-C(17)	116.8(2)	O(5)-S(2)-O(6)	118.25(12)
C(13)-C(12)-Se(2)	119.98(19)	O(5)-S(2)-C(17)	107.83(12)
C(17)-C(12)-Se(2)	123.22(19)	O(6)-S(2)-C(17)	107.52(12)
C(14)-C(13)-C(12)	122.2(2)	O(5)-S(2)-C(19)	107.55(12)
C(13)-C(14)-C(15)	120.0(2)	O(6)-S(2)-C(19)	108.23(12)
O(4)-C(15)-C(16)	125.3(2)	C(17)-S(2)-C(19)	106.96(12)
O(4)-C(15)-C(14)	115.2(2)	C(1)-Se(1)-Se(2)	102.08(8)
C(16)-C(15)-C(14)	119.5(2)	C(12)-Se(2)-Se(1)	102.13(7)

Single Crystal X-Ray Structure of Compound 117



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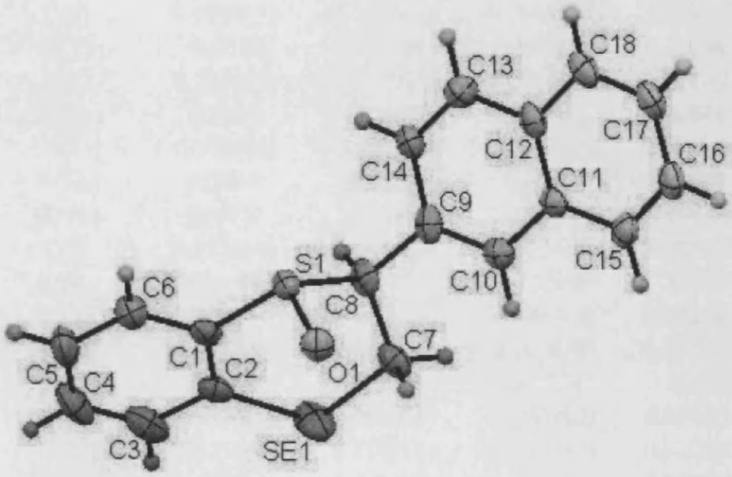

Table 1. Crystal data and structure refinement for Compound **117**.

Identification code	tw0913t		
Melting Point	114–116 °C	Absorption coefficient	2.689 mm^{-1}
Empirical formula	$C_{18}H_{14}OSSe$	F(000)	720
Formula Weight	357.31	Crystal size	0.40 x 0.08 x 0.04 mm^3
Temperature	150(2)	Theta range for data collection	3.04° to 26.06°
Wavelength	0.71073	Index ranges	-18<=h<=18
Creation method	SHELXL-97		-14<=k<=13
Crystal System	Monoclinic		-10<=l<=10
Space group	P21/c	Refections collected	4636
Unit cell dimensions	a = 15.0770(8) Å	Independent refections	2843 [R(int) = 0.0772]
	b = 12.1720(6) Å	Completeness to theta =26.06°	97.9%
	c = 8.3400(4) Å	Refinement method	Full-matrix least-squares on F^2
	α = 90.00°	Data / restraints / parameters	2843 / 0 / 191
	β = 105.993(2)°	Godness-of-fit on F^2	1.041
	γ = 90.00°	Final R indices[I >2sigma(I)]	R1 = 0.0833 wR2 = 0.1912
Volume	1471.29(13) $Å^3$	R indices (all data)	R1 = 0.1267 wR2 = 0.2175
Z	4	Largest diff. peak and hole	1.724 and -0.905 e. $Å^{-3}$
Density (calculated)	1.613 mg/cm^3		

Table 2. Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for compound **117**. U(eq) is defined as one third of the trace of the orthogonalised U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	0.1638(4)	0.2035(6)	0.0063(8)	0.0263(14)
C(2)	0.1182(4)	0.1078(6)	-0.0592(8)	0.0299(15)
C(3)	0.0237(5)	0.1151(8)	-0.1379(9)	0.045(2)
H(3)	-0.0091	0.0511	-0.1860	0.054
C(4)	-0.0220(5)	0.2115(8)	-0.1468(10)	0.047(2)
H(4)	-0.0865	0.2134	-0.1990	0.057
C(5)	0.0234(5)	0.3079(8)	-0.0811(11)	0.048(2)
H(5)	-0.0090	0.3756	-0.0906	0.058
C(6)	0.1170(5)	0.3027(6)	-0.0014(10)	0.0371(17)
H(6)	0.1492	0.3667	0.0478	0.044
C(7)	0.3026(4)	-0.0067(6)	0.0601(9)	0.0321(16)
H(7A)	0.3089	-0.0124	0.1812	0.038
H(7B)	0.3419	-0.0640	0.0307	0.038
C(8)	0.3354(4)	0.1052(6)	0.0224(9)	0.0288(15)
H(8)	0.3180	0.1177	-0.1008	0.035
C(9)	0.4391(4)	0.1230(6)	0.0962(8)	0.0285(15)
C(10)	0.4924(4)	0.0559(6)	0.2156(8)	0.0271(15)
H(10)	0.4660	-0.0085	0.2476	0.033
C(11)	0.5878(4)	0.0812(5)	0.2939(8)	0.0246(14)
C(12)	0.6250(4)	0.1782(6)	0.2423(9)	0.0305(15)
C(13)	0.5695(5)	0.2450(6)	0.1178(9)	0.0320(16)
H(13)	0.5946	0.3096	0.0837	0.038
C(14)	0.4792(4)	0.2178(6)	0.0449(9)	0.0298(15)
H(14)	0.4428	0.2629	-0.0413	0.036
C(15)	0.6440(5)	0.0161(6)	0.4200(9)	0.0326(16)
H(15)	0.6202	-0.0502	0.4518	0.039
C(16)	0.7327(5)	0.0467(6)	0.4977(10)	0.0365(17)
H(16)	0.7696	0.0023	0.5844	0.044
C(17)	0.7694(4)	0.1432(7)	0.4505(9)	0.0354(17)
H(17)	0.8308	0.1641	0.5068	0.042
C(18)	0.7183(4)	0.2076(6)	0.3247(9)	0.0339(16)
H(18)	0.7447	0.2718	0.2920	0.041
O(1)	0.2884(3)	0.1670(4)	0.2940(5)	0.0300(11)
S(1)	0.28278(10)	0.21233(13)	0.1252(2)	0.0251(4)
Se(1)	0.17349(5)	-0.03310(7)	-0.06386(12)	0.0496(4)

Table 3. Anisotropic displacement parameters ($Å^2$) for compound **117**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11}+...+2hka^*b^*U^{12}]$.

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	0.024(3)	0.039(4)	0.017(3)	0.006(3)	0.008(2)	-0.001(3)
C(2)	0.031(3)	0.036(4)	0.027(4)	-0.002(3)	0.015(3)	-0.006(3)
C(3)	0.034(4)	0.070(6)	0.032(4)	-0.010(4)	0.012(3)	-0.013(4)
C(4)	0.021(3)	0.084(7)	0.034(4)	-0.002(4)	0.003(3)	0.001(4)
C(5)	0.028(4)	0.063(6)	0.052(5)	0.015(4)	0.008(3)	0.015(4)
C(6)	0.031(3)	0.038(4)	0.042(4)	0.003(4)	0.010(3)	0.002(3)
C(7)	0.027(3)	0.040(4)	0.032(4)	-0.011(3)	0.013(3)	-0.001(3)
C(8)	0.030(3)	0.028(4)	0.030(4)	-0.012(3)	0.013(3)	0.007(3)
C(9)	0.030(3)	0.031(4)	0.022(3)	-0.010(3)	0.004(3)	0.009(3)
C(10)	0.032(3)	0.028(4)	0.024(4)	-0.005(3)	0.012(3)	0.000(3)
C(11)	0.025(3)	0.024(3)	0.029(4)	-0.004(3)	0.014(3)	0.003(3)
C(12)	0.027(3)	0.036(4)	0.032(4)	-0.005(3)	0.014(3)	0.008(3)
C(13)	0.040(4)	0.032(4)	0.027(4)	-0.001(3)	0.015(3)	0.003(3)
C(14)	0.022(3)	0.034(4)	0.032(4)	-0.001(3)	0.005(3)	0.002(3)
C(15)	0.036(4)	0.029(4)	0.036(4)	0.002(3)	0.016(3)	0.011(3)
C(16)	0.032(4)	0.037(4)	0.043(4)	-0.001(3)	0.014(3)	0.011(3)
C(17)	0.023(3)	0.050(5)	0.035(4)	-0.003(4)	0.010(3)	0.006(3)
C(18)	0.028(3)	0.038(4)	0.039(4)	-0.008(3)	0.014(3)	0.003(3)
O(1)	0.035(2)	0.037(3)	0.021(2)	-0.001(2)	0.0111(19)	0.003(2)
S(1)	0.0213(7)	0.0264(9)	0.0274(9)	-0.0024(7)	0.0062(6)	0.0003(6)
Se(1)	0.0375(5)	0.0398(6)	0.0705(7)	-0.0217(4)	0.0133(4)	-0.0114(3)

Table 4. Bond lengths [Å] for compound **117**.

Atoms	Distance [Å]	Atoms	Distance [Å]
C(1)-C(2)	1.386(10)	C(9)-C(10)	1.365(9)
C(1)-C(6)	1.390(10)	C(9)-C(14)	1.422(10)
C(1)-S(1)	1.798(6)	C(10)-C(11)	1.440(9)
C(2)-C(3)	1.398(10)	C(10)-H(10)	0.9500
C(2)-Se(1)	1.911(7)	C(11)-C(15)	1.400(9)
C(3)-C(4)	1.352(13)	C(11)-C(12)	1.424(10)
C(3)-H(3)	0.9500	C(12)-C(13)	1.400(10)
C(4)-C(5)	1.393(13)	C(12)-C(18)	1.431(9)
C(4)-H(4)	0.9500	C(13)-C(14)	1.370(9)
C(5)-C(6)	1.386(10)	C(13)-H(13)	0.9500
C(5)-H(5)	0.9500	C(14)-H(14)	0.9500
C(6)-H(6)	0.9500	C(15)-C(16)	1.368(10)
C(7)-C(8)	1.512(11)	C(15)-H(15)	0.9500
C(7)-Se(1)	1.962(6)	C(16)-C(17)	1.400(11)
C(7)-H(7A)	0.9900	C(16)-H(16)	0.9500
C(7)-H(7B)	0.9900	C(17)-C(18)	1.365(10)
C(8)-C(9)	1.529(9)	C(17)-H(17)	0.9500
C(8)-S(1)	1.855(6)	C(18)-H(18)	0.9500
C(8)-H(8)	1.0000	O(1)-S(1)	1.493(5)

Table 5. Angles [°] for compound **117**.

Atoms	Angle [°]	Atoms	Angle [°]
C(2)-C(1)-C(6)	121.5(6)	C(14)-C(9)-C(8)	117.8(6)
C(2)-C(1)-S(1)	125.3(5)	C(9)-C(10)-C(11)	121.1(6)
C(6)-C(1)-S(1)	113.0(5)	C(9)-C(10)-H(10)	119.4
C(1)-C(2)-C(3)	117.5(7)	C(11)-C(10)-H(10)	119.4
C(1)-C(2)-Se(1)	126.2(5)	C(15)-C(11)-C(12)	119.2(6)
C(3)-C(2)-Se(1)	116.2(6)	C(15)-C(11)-C(10)	122.8(6)
C(4)-C(3)-C(2)	121.3(8)	C(12)-C(11)-C(10)	117.9(6)
C(4)-C(3)-H(3)	119.4	C(13)-C(12)-C(11)	120.0(6)
C(2)-C(3)-H(3)	119.4	C(13)-C(12)-C(18)	121.2(7)
C(3)-C(4)-C(5)	121.5(7)	C(11)-C(12)-C(18)	118.7(6)
C(3)-C(4)-H(4)	119.3	C(14)-C(13)-C(12)	120.5(7)
C(5)-C(4)-H(4)	119.3	C(14)-C(13)-H(13)	19.8
C(6)-C(5)-C(4)	118.3(8)	C(12)-C(13)-H(13)	119.8
C(6)-C(5)-H(5)	120.8	C(13)-C(14)-C(9)	121.0(6)
C(4)-C(5)-H(5)	120.8	C(13)-C(14)-H(14)	119.5
C(5)-C(6)-C(1)	119.9(7)	C(9)-C(14)-H(14)	119.5
C(5)-C(6)-H(6)	120.0	C(16)-C(15)-C(11)	120.8(7)
C(1)-C(6)-H(6)	120.0	C(16)-C(15)-H(15)	119.6
C(8)-C(7)-Se(1)	111.9(5)	C(11)-C(15)-H(15)	119.6
C(8)-C(7)-H(7A)	109.2	C(15)-C(16)-C(17)	120.4(7)
Se(1)-C(7)-H(7A)	109.2	C(15)-C(16)-H(16)	119.8
C(8)-C(7)-H(7B)	109.2	C(17)-C(16)-H(16)	119.8
Se(1)-C(7)-H(7B)	109.2	C(18)-C(17)-C(16)	121.0(6)
H(7A)-C(7)-H(7B)	107.9	C(18)-C(17)-H(17)	119.5
C(7)-C(8)-C(9)	113.7(6)	C(16)-C(17)-H(17)	119.5
C(7)-C(8)-S(1)	109.3(5)	C(17)-C(18)-C(12)	119.8(7)
C(9)-C(8)-S(1)	103.5(4)	C(17)-C(18)-H(18)	120.1
C(7)-C(8)-H(8)	110.0	C(12)-C(18)-H(18)	120.1
C(9)-C(8)-H(8)	110.0	O(1)-S(1)-C(1)	106.6(3)
S(1)-C(8)-H(8)	110.0	O(1)-S(1)-C(8)	104.8(3)
C(10)-C(9)-C(14)	119.4(6)	C(1)-S(1)-C(8)	101.1(3)
C(10)-C(9)-C(8)	122.7(6)	C(2)-Se(1)-C(7)	102.5(3)

During this PhD-Thesis emerged the following publications:

Publications

D.M. Freudendahl, S.A. Shahzad, T. Wirth, **Recent Advances in Organoselenium Chemistry**, *Eur. J. Org. Chem.* **2009**, 1649–1664.

D. M. Freudendahl, S. Santoro, S. A. Shahzad, C. Santi, T. Wirth, **Green Chemistry with Selenium Reagents: Development of Efficient Catalytic Reactions**, *Angew. Chem. Int. Ed.* **2009**, *48*, 8409–8411.

U. Farooq, S. Schäfer, A. A. Shah, D. M. Freudendahl, T. Wirth, **Synthesis of New Enantiomerically Pure Organoiodine Catalysts and Their Application in the α–Functionalization of Ketones**, *Synthesis*, **2010**, *42*,

D. M. Freudendahl, M. Iwaoka, T. Wirth, **Synthesis of New Sulfoxide-Containing Diselenides and Unexpected Cyclization Reactions to 2,3-Dihydro-1,4-benzoselenothiine 1-Oxides**, *Eur. J. Org. Chem.* **2010**, 3934.

D. M. Freudendahl, T. Wirth, **New Selenium Electrophiles and Their Reactivity** in *Frontiers of Selenium and Tellurium Chemistry: From Small Molecules to Biomolecules and Materials*, Eds.: J. Derek Woolins, Risto Laitinen, Springer **2010**, submitted.

Poster Presentations:

D. M. Freudendahl, T. Wirth, "Selenium Electrophiles and Chiral Counteranions – A Good Match?", **RSC South West Regional Meeting**, 21.01.2009, Southampton, UK.

D. M. Freudendahl, T. Wirth, "A New Sulfoxide-Containing Diselenide and an Unexpected Cyclisation Reaction", **42nd IUPAC Congress: Chemistry Solutions**, 02.-07.08. 2009, Glasgow, UK.

D. M. Freudendahl, T. Wirth, "A New Sulfoxide-Containing Diselenide and an Unexpected Cyclisation Reaction", **11th International Conference on the Chemistry of Selenium and Tellurium (ICCST-11),** 01.08 - 06.08.2010, Oulu, Finland.

Oral Presentations:

D. M. Freudendahl, "ACDC and Selenium – Rock meets trace element", **Organic Chemistry Meeting 2009**, 22.06.2009, Cardiff, UK.

D. M. Freudendahl, "Syntheses of New Sulfoxide-Containing Diselenides and an Unexpected Cyclization Reaction", **SCI Symposium Bristol**, 25.03.2010, Bristol, UK.

D. M. Freudendahl, "Syntheses of New Sulfoxide-Containing Diselenides and an Unexpected Cyclization Reaction", **Cardiff Spring Conference 2010**, 05.-06.05.2010, Cardiff, UK. First prize for best presentation.

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